Lee, B.
10/077406

FILE 'REGISTRY' ENTERED AT 12:10:49 ON 23 SEP 2005
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STRUCTURE FILE UPDATES: 22 SEP 2005 HIGHEST RN 863708-11-6
DICTIONARY FILE UPDATES: 22 SEP 2005 HIGHEST RN 863708-11-6

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TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

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* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

-key terms

E LYMPHOTOXIN BETA RECEPTOR/CN 5
L25 1 S LYMPHOTOXIN BETA RECEPTOR?/CN

FILE 'CAPLUS' ENTERED AT 12:10:49 ON 23 SEP 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 23 Sep 2005 VOL 143 ISS 14
FILE LAST UPDATED: 22 Sep 2005 (20050922/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

Searcher : Shears 571-272-2528

This file contains CAS Registry Numbers for easy and accurate substance identification.

L25 1 SEA FILE=REGISTRY ABB=ON PLU=ON LYMPHOTOXIN BETA RECEPTOR?/CN
L26 279 SEA FILE=CAPLUS ABB=ON PLU=ON L25 OR (LYMPHOTOXIN OR LYMPHO TOXIN OR LT)(W)(BR OR (B OR BETA)(1W)(RECEPTOR OR R)) OR LTBR
L27 58 SEA FILE=CAPLUS ABB=ON PLU=ON L26(L)(ANTIBOD? OR FC(1A)(IMMUNOGLOBULIN OR IG OR IMMUNO GLOBULIN))
L28 27 SEA FILE=CAPLUS ABB=ON PLU=ON L27(L)(TREAT? OR THERAP? OR PREVENT?)
L29 0 SEA FILE=CAPLUS ABB=ON PLU=ON L28 NOT (PY=>1995 OR PD=>19950721) ← Restrict to hits dated prior to 07-21-95

L28 ANSWER 1 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 17 Jun 2005
ACCESSION NUMBER: 2005:524968 CAPLUS
DOCUMENT NUMBER: 143:58519
TITLE: Antibodies that specifically bind to TL5, a member of the TNF ligand superfamily, sequences thereof, and therapeutic and diagnostic uses
INVENTOR(S): Rosen, Craig A.; Ruben, Steven M.
PATENT ASSIGNEE(S): Human Genome Sciences, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 78 pp., Cont.-in-part of Appl. No. PCT/US03/10956.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005129614	A1	20050616	US 2004-943197	20040917
WO 2003089575	A2	20031030	WO 2003-US10956	20030410
WO 2003089575	A3	20041007		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-372087P P 20020415
WO 2003-US10956 A2 20030410

AB The present invention relates to **antibodies** and related mols. (e.g. scFv, monoclonal **antibody**, chimeric **antibodies**, or fragments) that specifically bind to TL5, a member of the TNF (tumor necrosis factor) ligand superfamily. In specific embodiments, the **antibodies** of the invention inhibit TL5 binding to a TL5 receptor (e.g., TNF receptors TR2, TR6, or **LT.beta.R**). Such **antibodies**

have uses, for example, in the **prevention** and **treatment** of cancer as well as immune system diseases and disorders including autoimmune disease, rheumatoid arthritis, graft rejection, graft vs. host disease, and lymphadenopathy. The invention also relates to nucleic acid mols. encoding anti-TL5 **antibodies**, vectors and host cells containing these nucleic acids, and methods for producing the same. The present invention relates to methods and compns. for **preventing**, detecting, diagnosing, **treating** or ameliorating a disorder, especially cancer as well as immune disorders, comprising administering to an animal, preferably a human, an effective amount of one or more **antibodies** that specifically bind to TL5.

L28 ANSWER 2 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 05 Apr 2005
ACCESSION NUMBER: 2005:291363 CAPLUS
DOCUMENT NUMBER: 142:480243
TITLE: Role of gut-associated lymphoreticular tissues in intestinal IgA immunity
AUTHOR(S): Yamamoto, Masafumi
CORPORATE SOURCE: Department of Oral Medicine, Nihon University School of Dentistry at Matsudo, Chiba, 271-8587, Japan
SOURCE: Journal of Oral Biosciences (2005), 47(1), 6-10
CODEN: JOBOA8; ISSN: 1349-0079
PUBLISHER: Japanese Association for Oral Biology
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Despite the fact that intestinal IgA responses are known to be regulated by gut-associated lymphoreticular tissues (GALT), the exact sites where this regulatory network is formed are only partially understood. Our study shows that antigen-specific intestinal IgA **antibodies** are induced after oral immunization in mice made deficient in Peyer's patches (PP) by in utero **treatment** with **lymphotoxin**-β **receptor** and Ig (**LT.beta.R**-Ig). These results suggest that the PP-independent pathways exist for antigen-specific intestinal IgA responses. On the other hand, postnatal **LTβ R**-Ig-**treated** mice lacking isolated lymphoid follicles (ILF) were still able to produce significant mucosal IgA responses. Furthermore, mice **treated** with both TNF receptor p55 and Ig (TNFR55-Ig) and **LT.beta.R**-Ig in utero, which lack PP and mesenteric lymph nodes (MLN) but retain intact ILF, failed to induce antigen-specific IgA responses after oral immunization. These findings demonstrated that ILF were not essential for induction of intestinal IgA responses. Interestingly, however, the IgA responses induced in the PP- or ILF- null mice were significantly lower than those seen in the control mice. Taken together, these findings suggest that aggregated lymphoid follicles residing in the intestinal lumen, e.g. PP and ILF, and draining MLN, may comprise an integrated regulatory network for the induction of maximum IgA **antibody** responses to orally administered antigens.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 3 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 16 Dec 2004
ACCESSION NUMBER: 2004:1076168 CAPLUS

TITLE: Absence of lymph nodes in NOD mice treated with lymphotoxin-β receptor immunoglobulin protects from diabetes
AUTHOR(S): Levisetti, Matteo G.; Suri, Anish; Frederick, Katherine; Unanue, Emil R.
CORPORATE SOURCE: Department of Medicine, Washington University School of Medicine, St. Louis, MO, USA
SOURCE: Diabetes (2004), 53(12), 3115-3119
CODEN: DIAEAZ; ISSN: 0012-1797
PUBLISHER: American Diabetes Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pregnant nonobese diabetic (NOD) mice were **treated** with **lymphotoxin**-β **receptor** Ig fusion protein (**LT.beta.R**-Ig) or control human Ig on days embryonic day 11 (E11) and E14, and offspring were followed for the development of anti-β-cell **antibodies**, islet pathol., and hyperglycemia. The development of anti-β-cell surface **antibodies** was abrogated in **treated** mice compared with controls. Autopsy examination of the mice at 30 wk of age revealed normal development of secondary lymphoid structures in the control animals; however, mice **treated** with **LT.beta.R**-Ig had no axillary, inguinal, popliteal, or peripancreatic lymph nodes. Histol. examination of the pancreata of the control mice revealed a severe and destructive mononuclear cellular infiltrate in the islets, whereas the islets of the **LT.beta.R**-Ig-**treated** mice were devoid of any insulitis. None of the **LT.beta.R**-Ig-**treated** mice (n = 22) developed diabetes; in contrast, 80% of the control mice (n = 46) developed diabetes at 1 yr of age. The **LT.beta.R**-Ig-**treated** mice did not contain diabetogenic T-cells. However, the **treated** mice developed diabetes upon inoculation with diabetogenic T-cells. In this model of spontaneous autoimmune diabetes, secondary lymphoid structures, most likely the peripancreatic lymph nodes, were essential for the development of pathol. anti-β-cell autoimmunity.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 4 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 09 Aug 2004
ACCESSION NUMBER: 2004:640215 CAPLUS
DOCUMENT NUMBER: 141:330468
TITLE: Lymphotoxin β receptor signaling induces the chemokine CCL20 in intestinal epithelium
AUTHOR(S): Rumbo, Martin; Sierro, Frederic; Debard, Nathalie; Kraehenbuhl, Jean-Pierre; Finke, Daniela
CORPORATE SOURCE: Lausanne Branch, Swiss Institute for Experimental Cancer Research, Epalinges, Switz.
SOURCE: Gastroenterology (2004), 127(1), 213-223
CODEN: GASTAB; ISSN: 0016-5085
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background & Aims: The follicle-associated epithelium (FAE) that overlies Peyer's patches (PPs) exhibits distinct features compared with the adjacent villus epithelium. Besides the presence of antigen-sampling membranous M cells and the down-regulation of digestive functions, it

constitutively expresses the chemokine CCL20. The mechanisms that induce FAE differentiation and CCL20 expression are poorly understood. The aim of this work was to test whether **lymphotoxin** . **beta. receptor** signaling (**LT.beta** .**R**), which plays a central role in PPs' organogenesis, mediates CCL20 gene expression in intestinal epithelial cells. Methods: CCL20, lymphotoxin β (LTβ) and **LT.** **beta.R** expression were monitored during embryonic development by in situ hybridization of mouse intestine. The human intestinal epithelial cell line T84 was used to study CCL20 expression following LTα1/β2 stimulation in vivo CCL20 expression following agonistic anti-**LT.beta.R** **antibody treatment** was studied by laser microdissection and quant. RT-PCR. Results: CCL20 was expressed in the FAE before birth at the time when the first hematopoietic CD4+CD3- appeared in the PP anlage. **LT.beta.R** was expressed in the epithelium during PP organogenesis, making it a putative target for LTα1β2 signals. In vitro, CCL20 was induced in T84 cells upon **LT.beta.R** signaling, either using an agonistic ligand or anti-**LT.** **beta. receptor** agonistic **antibody.** LTα1β2-induced CCL20 expression was NF-κB dependent. **LT.beta.R** signaling up-regulated CCL20 expression in the small intestinal epithelium in vivo. Conclusions: Our results show that **LT.beta.R** signaling induces CCL20 expression in intestinal epithelial cells, suggesting that this pathway triggers constitutive production of CCL20 in the FAE.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 5 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 27 Jul 2004
ACCESSION NUMBER: 2004:597806 CAPLUS
DOCUMENT NUMBER: 141:172737
TITLE: Blocking of lymphotoxin-β receptor pathway in chronic colitis causes downregulation of MadCAM-1 and reduced leukocyte-endothelial cell interaction
AUTHOR(S): Janotta, M.; Stopfer, P.; Maennel, D. N.; Hehlgans, T.; Hornung, M.; Geissler, E.; Schlitt, H. J.; Farkas, S.
CORPORATE SOURCE: Klinik und Poliklinik fuer Chirurgie, Universitaet Regensburg, Germany
SOURCE: Chirurgisches Forum fuer Experimentelle und Klinische Forschung (2004) 241-243
CODEN: CFEKA7; ISSN: 0303-6227
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: German

AB The **lymphotoxin**-β **receptor** (**LT.beta.R**) pathway is critical for maintenance of organized lymphoid structures and involved in development of colitis as shown in different mouse colitis models. Thus, the mechanisms by which **LT.beta.R** activation contributes to the pathol. the chronic form of DSS-colitis was investigated. Moreover, it was demonstrated that mucosal addressin cell adhesion mol.-1 (MadCAM-1), which is strongly expressed in inflamed intestinal mucosa, plays a significant role in development

of chronic DSS-colitis. Acute colitis was induced in Balb/c mice (20 ± 0.4g; n = 10 per group) by oral administration of 5% dextran sodium sulfate (DSS) dissolved in drinking water for 4 cycles of **treatment**. Two weeks after completion of 4 cycles of DSS **treatment**, mice in the **therapy** group received 100 μg i.p. of a monoclonal **antibody** against **LT.beta.R** for 6 days. Mice of the control group received 100μg of an isotype **antibody**. To prepare mice for cell injection, a venous and arterial catheter was implanted in anesthetized animals. The colon was then mobilized and extriorized for in vivo microscopy. Leukocyte-endothelium interaction in collecting and postcapillary venules was visualized and quantified by epiillumination at a 680-fold magnification. For in vivo microscopy of the mucosa the colon was incised and leukocyte extravasation was calculated Then tissue was taken out for histol. and immunohistochem. tests. **Treatment** of chronic form of DSS-induced colitis with **LT.beta.R**-Ig significantly attenuated the development and histol. manifestation of the disease. The expression of the proinflammatory cytokines TNF, IL-1β and IL-6 was clearly reduced by **LT.beta.R**-Ig **treatment** in the chronic form of colitis. Moreover **LT .beta.R**-Ig **treatment** significantly downregulated MadCAM-1 expression, leading to reduced leukocyte endothelium interaction. Addnl., reduced extravasation of leukocytes to intestinal mucosa was observed MadCAM expression was semi-quant. detected by immunhistochem. The authors' results show, that **LT.beta.R** pathway inhibition leads to a downregulation of MadCAM-1 expression. This leads to a significant reduction of leukocyte-endothelium interaction, extravasation of lymphocytes and also to a better histol. score. This study verifies the pathophysiol. role of **LT.beta.R** pathway inhibition in the rise of inflammatory bowel disease, that is mediated by MadCAM-1.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 6 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 15 Jul 2004
ACCESSION NUMBER: 2004:566557 CAPLUS
DOCUMENT NUMBER: 141:105261
TITLE: Multivalent anti-**lymphotoxin** . **beta. receptor antibody** agonists for cancer diagnosis and **therapy**
INVENTOR(S): Garber, Ellen; Bailly, Veronique; Browning, Jeffrey L.
PATENT ASSIGNEE(S): Biogen Idec Ma Inc., USA
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058191	A2	20040715	WO 2003-US41393	20031222

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,

GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP,
KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,
DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-435154P P 20021220

AB Multivalent **antibody** constructs that are specific for human **lymphotoxin β receptor**, as well as their use in **treating** cancer and inhibiting tumor volume in a subject are disclosed. The multivalent **antibody** is either monospecific or bispecific, and can be used in combination with chemotherapeutic agent in cancer **therapy**.

L28 ANSWER 7 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 14 May 2004
ACCESSION NUMBER: 2004:392486 CAPLUS
DOCUMENT NUMBER: 140:405482
TITLE: Trimeric binding proteins for inhibition of trimeric cytokine binding to receptor and for treatment of cytokine-mediated diseases
INVENTOR(S): Holtet, Thor Las; Andersen, Mikkel Holmen
PATENT ASSIGNEE(S): Borean Pharma A/s, Den.; Ottow, Helle Krogh
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039841	A2	20040513	WO 2003-DK735	20031029
WO 2004039841	A3	20040910		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2503697	AA	20040513	CA 2003-2503697	20031029
EP 1558640	A2	20050803	EP 2003-769251	20031029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: DK 2002-1634 A 20021029
US 2002-421807P P 20021029

WO 2003-DK735 W 20031029

AB The present invention pertains to the provision of trimeric binding units which bind to trimeric cytokines. In particular there is provided a trimeric polypeptide, e.g. antibody and fragment or cytokine receptor polypeptide, comprising a trimerizing domain and three monomers with binding members capable of binding a trimeric cytokine. Preferably, the trimeric binding units bind in a manner such that upon binding, all receptor binding sites of the trimeric cytokine are substantially blocked, and hence the potential biol. activity of the trimeric cytokine is suppressed. In one aspect the invention relates to trimeric binders capable of binding to trimeric cytokines of the tumor necrosis factor ligand superfamily, such as TNF, TRAIL, RANKL, TWEAK, APRIL and BAFF. Thus, trimeric antibodies (e.g. D2E7 and CDP 870) and fragments specific to the TNF ligand superfamily, and trimeric proteins derived from TNF receptor superfamily members are used for inhibiting TNF binding to TNF receptor and for treating TNF-mediated diseases such as rheumatoid arthritis, psoriasis and Crohn's disease.

L28 ANSWER 8 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 14 May 2004
ACCESSION NUMBER: 2004:392443 CAPLUS
DOCUMENT NUMBER: 140:405481
TITLE: Anti-human **lymphotoxin B receptor (LTBR) antibodies** and fragments or lymphotoxin pathway inhibitors for **treatment** of immunological renal disorders
INVENTOR(S): Gommerman, Jennifer; Browning, Jeffrey L.
PATENT ASSIGNEE(S): Biogen, Inc., USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039329	A2	20040513	WO 2003-US34813	20031031
WO 2004039329	A3	20040715		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2505852	AA	20040513	CA 2003-2505852	20031031
EP 1565214	A2	20050824	EP 2003-781666	20031031
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: US 2002-422588P P 20021031

WO 2003-US34813 W 20031031

AB The disclosure relates to **treatment** of immunol. disorders, including but not limited to renal disorders associated with Ig deposits. The disclosure further relates to the lymphotoxin pathway. Compns. comprising lymphotoxin pathway inhibitors, especially **antibodies** or fragments specific to **LTBR** are described. The invention also disclosed inhibitory fusion protein comprising soluble **LTBR** and one or more heterologous protein domains, as well as method of evaluating efficacy of a compound for **treatment** of IgA nephropathy and nucleic acid hybridization method for detecting polypeptides inhibiting Ig. secretion by B cells.

L28 ANSWER 9 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 11 Jan 2004
ACCESSION NUMBER: 2004:20451 CAPLUS
DOCUMENT NUMBER: 140:92582
TITLE: Humanized anti-**lymphotoxin .beta . receptor antibodies** for cancer diagnosis and **therapy**
INVENTOR(S): Garber, Ellen; Simon, Kenneth; Saldanha, Jose
PATENT ASSIGNEE(S): Biogen, Inc., USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002431	A2	20040108	WO 2003-US20762	20030701
WO 2004002431	A3	20040826		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2491480	AA	20040108	CA 2003-2491480	20030701
EP 1539793	A2	20050615	EP 2003-762296	20030701
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.:
US 2002-392993P P 20020701
US 2002-417372P P 20021009
WO 2003-US20762 W 20030701

AB This invention concerns humanized derivs. of mouse BHA10 monoclonal anti-**lymphotoxin beta receptor antibody**, cell lines that produce these **antibodies**,

immunochems. made from the **antibodies**, and diagnostic methods that use the **antibodies**. The invention also relates to the use of the **antibodies** alone or in combination with chemotherapeutic agent(s) in **therapeutic** methods.

L28 ANSWER 10 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 31 Oct 2003
ACCESSION NUMBER: 2003:856023 CAPLUS
DOCUMENT NUMBER: 139:349660
TITLE: Antibodies specific to TL5 for diagnosis, prognosis and treatment of cancer, immune and autoimmune disease, inflammation and lymphadenopathy
INVENTOR(S): Rosen, Craig A.; Ruben, Steven M.
PATENT ASSIGNEE(S): Human Genome Sciences, Inc., USA
SOURCE: PCT Int. Appl., 189 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003089575	A2	20031030	WO 2003-US10956	20030410
WO 2003089575	A3	20041007		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2481401	AA	20031030	CA 2003-2481401	20030410
EP 1499353	A2	20050126	EP 2003-728362	20030410
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005129614	A1	20050616	US 2004-943197	20040917
PRIORITY APPLN. INFO.:			US 2002-372087P	P 20020415
			WO 2003-US10956	W 20030410

AB The present invention relates to antibodies and related mols. (e.g. scFv, monoclonal antibody, humanized or chimeric antibodies, or fragments) that specifically bind to TL5. Such antibodies have uses, for example, in the prevention and treatment of cancer as well as immune system diseases and disorders including autoimmune disease, rheumatoid arthritis, graft rejection, graft vs. host disease, and lymphadenopathy. The invention also relates to nucleic acid mols. encoding anti-TL5 antibodies, vectors and host cells containing these nucleic acids, and methods for producing the same. The present invention relates to methods and compns. for preventing, detecting, diagnosing, treating or ameliorating a disease or disorder, especially cancer as well as immune system diseases and disorders including autoimmune disease, rheumatoid arthritis, graft rejection, graft vs.

host disease, and lymphadenopathy, comprising administering to an animal, preferably a human, an effective amount of one or more antibodies or fragments or variants thereof, or related mols., that specifically bind to TL5.

L28 ANSWER 11 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 15 Aug 2003
ACCESSION NUMBER: 2003:633902 CAPLUS
DOCUMENT NUMBER: 139:173769
TITLE: Composition and method for modulating an inflammatory response
INVENTOR(S): Kuai, Jun; Wooters, Joseph L.; Nickbarg, Elliott B.; Qiu, Yongchang; Lin, Lih-ling
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003066834	A2	20030814	WO 2003-US3923	20030210
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004038299	A1	20040226	US 2003-361270	20030210
PRIORITY APPLN. INFO.:			US 2002-355183P	P 20020208

AB The invention relates to compns. and methods comprising **lymphotoxin-beta receptor** (**LT.beta.R**) modulators, which activate or inhibit **LT.beta.R** signaling. **LT.beta.R** modulators are useful for **treating** lymphocyte-mediated immunol. diseases and cancer, and more particularly, for regulating mitochondrial-mediated apoptosis. This invention relates to soluble forms of the **LTβR** complex proteins that act as **LTβR** activating or inhibiting agents. This invention also relates to the use of soluble mols., directed against either the **LT.beta.R**, its ligands, LIGHT and LTβ1α2, or its intracellular binding partners, that function to regulate **LT.beta.R** signaling. A novel screening method for selecting soluble receptors, **antibodies** and other agents that modulate **LT.beta.R** signaling is provided.

L28 ANSWER 12 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 01 Jul 2003
ACCESSION NUMBER: 2003:499883 CAPLUS

DOCUMENT NUMBER: 139:83843
TITLE: Lymphotoxin β receptor-Ig fusion protein treatment blocks actively induced, but not adoptively transferred, uveitis in Lewis rats
AUTHOR(S): Shao, Hui; Fu, Yangxin; Song, Lei; Sun, Sheher; Kaplan, Herry J.; Sun, Deming
CORPORATE SOURCE: Department of Ophthalmology and Visual Sciences, Kentucky Lions Eye Center, University of Louisville, Louisville, USA
SOURCE: European Journal of Immunology (2003), 33(6), 1736-1743
CODEN: EJIMAF; ISSN: 0014-2980
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Previous studies have shown that treatment of rodents with a lymphotoxin (LT) β receptor-Ig fusion protein (LTβR-Ig), which binds to both LT and LIGHT, prevents the development of autoimmune diseases, but the mechanism involved is unclear. To explore the potential role of LT or LIGHT in the pathogenesis of autoimmune uveitis, uveitis was induced in Lewis rats either by immunization with an uveitogenic peptide, R16, derived from the interphotoreceptor retinoid-binding protein, or by adoptive transfer of R16-specific T cells. Interestingly, LTβR-Ig treatment completely prevented actively induced uveitis, but not the adoptively transferred disease. We also show that LTβR-Ig-treated R16-injected rats had a significantly decreased T cell response to R16 and that herpesvirus entry mediator (HVEM)-Ig, a fusion protein that blocks LIGHT, also inhibited disease development. Our results suggest that LT or LIGHT plays a critical role in the induction, rather than the effector, phase of the disease.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 13 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 15 Jun 2003
ACCESSION NUMBER: 2003:455250 CAPLUS
DOCUMENT NUMBER: 139:270896
TITLE: Follicular dendritic cell dedifferentiation by treatment with an inhibitor of the lymphotoxin pathway dramatically reduces scrapie susceptibility
AUTHOR(S): Mabbott, Neil A.; Young, Janice; McConnell, Irene; Bruce, Moira E.
CORPORATE SOURCE: Neuropathogenesis Unit, Inst. for Animal Health, Edinburgh, EH9 3JF, UK
SOURCE: Journal of Virology (2003), 77(12), 6845-6854
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Transmissible spongiform encephalopathies (TSEs) may be acquired peripherally, in which case infectivity usually accumulates in lymphoid tissues before dissemination to the nervous system. Studies of mouse scrapie models have shown that mature follicular dendritic cells (FDCs), expressing the host prion protein (PrPc), are critical for replication of infection in lymphoid tissues and subsequent neuro-invasion. Since FDCs require lymphotoxin signals from B

lymphocytes to maintain their differentiated state, blockade of this stimulation with a lymphotoxin β receptor-Ig fusion protein (LTβR-Ig) leads to their temporary differentiation. Here, a single treatment with LTβR-Ig before i.p. scrapie inoculation blocked the early accumulation of in effectivity and disease-specific PrP (PrPSc) within the spleen and substantially reduced disease susceptibility. These effects coincided with an absence of FDCs in the spleen for ca. 28 days after treatment. Although the period of FDC dedifferentiation was extended to at least 49 days by consecutive LTβR-Ig treatments, this had little added protective benefit after injection with a moderate dose of scrapie. The authors also demonstrate that mature FDCs are critical for the transmission of scrapie from the gastrointestinal tract. Treatment with LTβR-Ig before oral scrapie inoculation blocked PrPSc accumulation in Peyer's patches and mesenteric lymph nodes and prevented neuro-invasion. However, treatment 14 days after oral inoculation did not affect survival time or susceptibility, suggesting that in effectivity may have already spread to the peripheral nervous system. Although manipulation of FDCs may offer a potential approach for early intervention in peripherally acquired TSEs, these data suggest that the duration of the treatment window may vary widely depending on the route of exposure.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 14 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 11 Jun 2003
ACCESSION NUMBER: 2003:447582 CAPLUS
DOCUMENT NUMBER: 139:228831
TITLE: A simple method for enriching populations of transfected CHO cells for cells of higher specific productivity
AUTHOR(S): Brezinsky, S. C. G.; Chiang, G. G.; Szilvasi, A.; Mohan, S.; Shapiro, R. I.; MacLean, A.; Sisk, W.; Thill, G.
CORPORATE SOURCE: Biogen Inc., Cambridge, MA, 02142, USA
SOURCE: Journal of Immunological Methods (2003), 277(1-2), 141-155
CODEN: JIMMBG; ISSN: 0022-1759
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To establish a simple and rapid method for the screening of stable recombinant Chinese hamster ovary (CHO) cell lines, the authors have developed a cell surface labeling technique using fluorescently tagged **antibodies** that bind to secreted target proteins at low temperature Using fluorescence intensity as the sole criterion for selection of cells, the authors are able to enrich populations of highly productive cells using preparative flow cytometry sorting. Reiterative sorting based on selection of cells having the highest fluorescence intensity of cell surface labeled protein results in dramatic increases in specific cellular productivity. Using **lymphotoxin-beta receptor** IgG fusion protein as a model system, the authors have demonstrated a greater than 20-fold increase in specific productivity (0.49-11.5 pg cell-1 day-1) (pcd) without the use of methotrexate (MTX)-mediated selection or amplification. In addition, the flow cytometry used to enrich for and clone high producer cell lines has reduced development time by more than 50% and the number

of screening assays by more than 10-fold. When a transfected population of CHO cells expressing a humanized version of the murine monoclonal **antibody** (mAb) AQC2 directed against human alpha 1 beta 1 integrin was subjected to the same **treatment**, a 25-fold improvement in specific productivity (0.3-8.0 pcd) was observed Furthermore, similar application of this technique to MTX-amplified clones resulted in up to 120-fold overall improvement in specific productivity (up to 42 pcd). Greater than 20 examples are also presented to demonstrate the robustness and performance of this technique.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 15 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 13 Jun 2002
ACCESSION NUMBER: 2002:444385 CAPLUS
DOCUMENT NUMBER: 137:24297
TITLE: Soluble lymphotoxin-β receptors as therapeutic agents for the treatment of immunological disease
INVENTOR(S): Browning, Jeffrey L.; Benjamin, Christopher D.; Hochman, Paula S.
PATENT ASSIGNEE(S): Biogen, Inc., USA
SOURCE: U.S., 27 pp., Cont.-in-part of U.S. 5,925,351. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6403087	B1	20020611	US 1998-166	19980608
US 5925351	A	19990720	US 1995-505606	19950721
WO 9703687	A1	19970206	WO 1996-US12010	19960719
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
NZ 503818	A	20010831	NZ 1996-503818	19960719
EP 1488799	A2	20041222	EP 2004-17208	19960719
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
US 2005037003	A1	20050217	US 2002-77406	20020215

PRIORITY APPLN. INFO.:		
US 1995-505606	A2	19950721
WO 1996-US12010	W	19960719
EP 1996-925393	A3	19960719
NZ 1996-313441	A1	19960719
US 1998-166	A3	19980608

AB This invention relates to compns. and methods comprising " **lymphotoxin-β receptor** blocking

Searcher : Shears 571-272-2528

agents" which block **lymphotoxin**-β **receptor** signaling. **Lymphotoxin**-β **receptor** blocking agents are useful for **treating** lymphocyte-mediated immunol. diseases, and more particularly, for inhibiting Th1 cell-mediated immune responses. This invention relates to soluble forms of the **lymphotoxin**-β **receptor** extracellular domain that act as **lymphotoxin** -β **receptor** blocking agents. This invention also relates to the use of **antibodies** directed against either the **lymphotoxin**-β **receptor** or its ligand, surface lymphotoxin, that act as **lymphotoxin** -β **receptor** blocking agents. A novel screening method for selecting soluble receptors, **antibodies** and other agents that block **LT**-β **receptor** signaling is provided.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 16 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 19 Apr 2002
ACCESSION NUMBER: 2002:293705 CAPLUS
DOCUMENT NUMBER: 136:324074
TITLE: Humanized anti-**lymphotoxin .beta** . **receptor (LT-.beta** .-**R) antibodies** for **treating** tumor
INVENTOR(S): Garber, Ellen; Lyne, Paul; Saldanha, Jose W.
PATENT ASSIGNEE(S): Biogen, Inc., USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030986	A2	20020418	WO 2001-US32140	20011012
WO 2002030986	A3	20030313		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2425809	AA	20020418	CA 2001-2425809	20011012
AU 2002011747	A5	20020422	AU 2002-11747	20011012
EP 1326897	A2	20030716	EP 2001-979824	20011012
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EE 200300179	A	20030815	EE 2003-179	20011012
TR 200300478	T2	20041021	TR 2003-200300478	20011012
JP 2004532608	T2	20041028	JP 2002-534371	20011012

CN 1547590	A	20041117	CN 2001-820591		20011012
NO 2003001642	A	20030613	NO 2003-1642		20030410
US 2004058394	A1	20040325	US 2003-412406		20030410
ZA 2003003347	A	20041117	ZA 2003-3347		20030430
BG 107802	A	20040130	BG 2003-107802		20030512
PRIORITY APPLN. INFO.:			US 2000-240285P	P	20001013
			US 2001-275289P	P	20010313
			US 2001-299987P	P	20010621
			WO 2001-US32140	W	20011012

AB LT-α-R-specific humanized murine CBE11 antibodies and fragments are provided. The humanized antibodies of this invention are linked to an immunotoxin (e.g. ricin A chain of Pseudomonas toxin), chemotherapeutic agent (e.g. adriamycin, 5-FU, vinblastine, actinomycin D, etoposide, cisplatin, methotrexate and doxorubicin), a radioisotope, or a cytotoxic factor (e.g. TNF-α, TNF-β, IL-1, INF-γ, and IL-2) for treating cancer in human patients.

L28 ANSWER 17 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 27 Mar 2001
ACCESSION NUMBER: 2001:214679 CAPLUS
DOCUMENT NUMBER: 134:365526
TITLE: Defective lymphotoxin-β receptor-induced NF-κB transcriptional activity in NIK-deficient mice
AUTHOR(S): Yin, Li; Wu, Lin; Wesche, Holger; Arthur, Cora D.; White, J. Michael; Goeddel, David V.; Schreiber, Robert D.
CORPORATE SOURCE: Center Immunology, Dep. Pathology and Immunology, Washington Univ. Sch. Med., St. Louis, MO, 63110, USA
SOURCE: Science (Washington, DC, United States) (2001), 291(5511), 2162-2165
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of NF-κB-inducing kinase (NIK) in cytokine signaling remains controversial. To identify the physiol. functions of NIK, the authors disrupted the NIK locus by gene targeting. Although NIK-/- mice displayed abnormalities in both lymphoid tissue development and **antibody** responses, NIK-/- cells manifested normal NF-κB DNA binding activity when **treated** with a variety of cytokines, including tumor necrosis factor (TNF), interleukin-1 (IL-1), and lymphotoxin-β (LTβ). However, NIK was selectively required for gene transcription induced via ligation of **LTβ receptor** but not TNF receptors. Thus, NIK regulates the transcriptional activity of NF-κB in a receptor-restricted manner.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 21 Apr 2000

ACCESSION NUMBER: 2000:260054 CAPLUS
DOCUMENT NUMBER: 132:292716
TITLE: Reversal of viral-induced systemic shock and respiratory distress by blockade of the lymphotoxin β pathway
INVENTOR(S): Browning, Jeff; Puglielli, Maryann; Ahmed, Rafi
PATENT ASSIGNEE(S): Biogen, Inc., USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000021558	A1	20000420	WO 1999-US23477		19991008
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2344049	AA	20000420	CA 1999-2344049		19991008
AU 9962964	A1	20000501	AU 1999-62964		19991008
AU 777492	B2	20041021			
EP 1119370	A1	20010801	EP 1999-950270		19991008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
BR 9915025	A	20010814	BR 1999-15025		19991008
TR 200100974	T2	20011121	TR 2001-200100974		19991008
EE 200100211	A	20020815	EE 2001-211		19991008
JP 2002527403	T2	20020827	JP 2000-575531		19991008
NZ 510560	A	20030926	NZ 1999-510560		19991008
NO 2001001757	A	20010608	NO 2001-1757		20010406
US 2002001585	A1	20020103	US 2001-829031		20010409
US 2004198635	A1	20041007	US 2004-829720		20040421
PRIORITY APPLN. INFO.:			US 1998-103662P	P	19981009
			WO 1999-US23477	W	19991008
			US 2001-829031	B1	20010409

AB This invention provides methods of inducing an antiviral response in an individual comprising administering to the individual an effective amount of a LT-β blocking agent and a pharmaceutically acceptable carrier. In particular this invention provides methods for **treating** viral-induced systemic shock and respiratory distress. The LT-β inhibitor is an anti-LT-β **antibody**, soluble **LT-β receptor**, or fusion protein containing **LT-β receptor** and Ig.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 19 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 23 Dec 1998
ACCESSION NUMBER: 1998:801597 CAPLUS
DOCUMENT NUMBER: 130:208275
TITLE: Both the lymphotoxin and tumor necrosis factor pathways are involved in experimental murine models of colitis
AUTHOR(S): MacKay, Fabienne; Browning, Jeffrey L.; Lawton, Pornsri; Shah, Samir A.; Comiskey, Martina; Bhan, Atul K.; Mizoguchi, Emiko; Terhorst, Cox; Simpson, Stephen J.
CORPORATE SOURCE: Department of Immunology, Inflammation and Cell Biology, Biogen, Cambridge, USA
SOURCE: Gastroenterology (1998), 115(6), 1464-1475
CODEN: GASTAB; ISSN: 0016-5085
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Membrane lymphotoxin (LT) α/β, a member of the tumor necrosis factor (TNF) family of immune regulatory mols., is involved both in the development of secondary lymphoid tissues and the maintenance of organized lymphoid tissues in the adult. Defects observed in the mucosal immune system in animals with a genetically disrupted LTα/β pathway coupled with the expression of LTα/β in activated T cells motivated an examination of the importance of this pathway in exptl. colitis. Soluble **LT. beta. receptor** (**LTβ R**) Ig fusion protein was used to inhibit the LTα/β axis in two independent rodent models of colitis: CD45RBhi CD4+-reconstituted SCID mice and bone marrow-transplanted tgε26 mice (BM → tgε26). **Treatment** with **LT.beta.R** Ig attenuated the development of both the clin. and histol. manifestations of the disease in these two murine models of colitis. Given the success of TNF inhibitors in the **treatment** of human Crohn's disease, the effects of **LT.beta.R** Ig have been compared with **antibody** to TNF in the BM → tgε26 model, and both **treatments** were equally efficacious. The LT pathway plays a role in the development of colitis as important as that of the TNF system and, therefore, represents a potential novel intervention point for the **treatment** of inflammatory bowel disease.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 20 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 12 Aug 1998
ACCESSION NUMBER: 1998:500119 CAPLUS
DOCUMENT NUMBER: 129:229478
TITLE: Lymph node genesis is induced by signaling through the lymphotoxin β receptor
AUTHOR(S): Rennert, Paul D.; James, Danelle; Mackay, Fabienne; Browning, Jeffrey L.; Hochman, Paula S.
CORPORATE SOURCE: Department of Immunology and Inflammation Biogen, Incorporated, Cambridge, MA, 02142, USA
SOURCE: Immunity (1998), 9(1), 71-79
CODEN: IUNIEH; ISSN: 1074-7613
PUBLISHER: Cell Press

DOCUMENT TYPE: Journal
LANGUAGE: English
AB We investigated lymphotoxin (LT) and TNF function in lymph node genesis and cellular organization by manipulating **LT.beta.-R** and TNF-R signaling. Lymph nodes developed in LTα-/- mice **treated** in utero with agonist anti-**LTβ -R** monoclonal **antibody.** Thus, **LTβ -R** signaling mediates lymph node genesis. Surprisingly, mucosal lymph nodes that can develop independently of LTαβ/ **LTβ -R** interaction were generated. Normal mice **treated** in utero with **LTβ -R**-Ig and TNF-R55-Ig or anti-TNF lacked all lymph nodes, indicating that TNF signaling contributes to lymph node genesis. Lymph nodes generated in LTα-/- mice had disrupted cellular organization. Therefore, **LTβ -R** signaling during gestation is not sufficient to establish normal cellular microarchitecture. We conclude that LT and TNF play critical roles in the genesis and cellular organization of lymph nodes.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 21 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 11 May 1998
ACCESSION NUMBER: 1998:268386 CAPLUS
DOCUMENT NUMBER: 129:3859
TITLE: Soluble **lymphotoxin-beta receptors,** anti-lymphotoxin receptor **antibodies,** and anti-lymphotoxin ligand **antibodies** as **therapeutic** agents for the **treatment** of immunological diseases
INVENTOR(S): Browning, Jeffrey; Hochman, Paula Susan; Rennert, Paul D.; Mackay, Fabienne
PATENT ASSIGNEE(S): Biogen, Inc., USA; Browning, Jeffrey; Hochman, Paula Susan; Rennert, Paul D.; Mackay, Fabienne
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9817313	A2	19980430	WO 1997-US19436	19971024
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2269614	AA	19980430	CA 1997-2269614	19971024
AU 9850896	A1	19980515	AU 1998-50896	19971024
AU 726357	B2	20001102		

BR 9712670	A	19991019	BR 1997-12670		19971024
EP 954333	A2	19991110	EP 1997-913798		19971024
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
CN 1237910	A	19991208	CN 1997-199906		19971024
NZ 335353	A	20000929	NZ 1997-335353		19971024
JP 2001502697	T2	20010227	JP 1998-519688		19971024
NO 9901926	A	19990625	NO 1999-1926		19990422
KR 2000052800	A	20000825	KR 1999-703619		19990424
BG 63565	B1	20020531	BG 1999-103416		19990520
US 2002197254	A1	20021226	US 2001-3211		20011031
PRIORITY APPLN. INFO.:			US 1996-29060P	P	19961025
			WO 1997-US19436	W	19971024
			US 1999-299139	A1	19990423

AB Compns. and methods comprising "lymphotoxin-β receptor blocking agents" which block lymphotoxin-β receptor signalling and are useful for altering immunol. diseases, and particularly antibody mediated immune responses. The lymphotoxin-β receptor blocking agents are monoclonal antibodies, soluble lymphotoxin-β receptor, anti-lymphotoxin ligand antibodies, or fusion protein of soluble lymphotoxin-β receptor and Ig Fc domain. The immunol. disease is e.g. AIDS, HIV infection, graft rejection, etc. Antiviral agent, anti-AIDS agent, or anti-CD40L and other carrier or adjuvant are also included in the remedy.

L28 ANSWER 22 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 11 Sep 1997
ACCESSION NUMBER: 1997:579823 CAPLUS
DOCUMENT NUMBER: 127:201749
TITLE: Cloning of cDNA for a novel tumor necrosis factor (TNF) receptor-associated factor TRAF5 and characterization of the gene product
INVENTOR(S): Nakata, Motomi; Nakano, Hiroyasu; Yagita, Hideo; Okumura, Ko
PATENT ASSIGNEE(S): Nakata, Motomi, Japan; Nakano, Hiroyasu; Yagita, Hideo; Okumura, Ko; Sumitomo Electric Industries, Ltd.
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9731110	A1	19970828	WO 1997-JP512		19970224
W: JP, US					
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
EP 882790	A1	19981209	EP 1997-903599		19970224
R: CH, DE, FR, GB, LI					
US 6426403	B1	20020730	US 1998-138277		19980818
PRIORITY APPLN. INFO.:			JP 1996-34674	A	19960222
			WO 1997-JP512	W	19970224

AB The cDNA encoding a novel member of the TRAF family, TRAF5, was isolated by PCR using the oligonucleotide primers derived from the conserved domains of the known TRAF members. It was isolated from mouse B-cell lymphoma cell A20.25 and human HAT109 cell, resp. TRAF5 shows specific affinity to **lymphotoxin**-β **receptor** (**LT**-**.beta.R**) and CD30, but not to CD40 or TNF-R2. It also exhibit the leucine zipper motif or the coiled structure. Expression of TRAF5 in various tissues was observed The antisense oligonucleotides of the cDNA and the **antibodies** to its encoded protein are useful for elucidating the signal transducer system of the TNF-R family. Furthermore, it is also useful in developing diagnostics and **therapeutics**.

L28 ANSWER 23 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 21 Aug 1997
ACCESSION NUMBER: 1997:534131 CAPLUS
DOCUMENT NUMBER: 127:219346
TITLE: Lymphotoxin but not tumor necrosis factor functions to maintain splenic architecture and humoral responsiveness in adult mice
AUTHOR(S): Mackay, Fabienne; Majeau, Gerard R.; Lawton, Pornsri; Hochman, Paula S.; Browning, Jeffrey L.
CORPORATE SOURCE: Department Immunology, Inflammation Cell Biology, Biogen, Cambridge, MA, 02142, USA
SOURCE: European Journal of Immunology (1997), 27(8), 2038-2042
CODEN: EJIMAF; ISSN: 0014-2980
PUBLISHER: Wiley-VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To compare the function of the tumor necrosis factor (TNF) and lymphotoxin (LT)α/β systems in the mature immune system, these 2 pathways were blocked with soluble receptor-Ig (R-Ig) fusion proteins in normal adult mice. Inhibition of LTα/β signaling using **LT.beta.R**-Ig or a blocking monoclonal **antibody** against murine LTβ had profound effects. The spleen lacked discrete B cell follicles and the marginal zone was altered. Less marked changes were detected in lymph nodes. LTα/β inhibition also **prevented** germinal center formation in the spleen and impaired Ig production in response to sheep red blood cells (SRBC) immunization. These results show that the LTα/β system is required for the maintenance of splenic architecture and normal immune responses, and not simply for the development of peripheral immune organs during ontogeny. In contrast, inhibition of the TNF/LTα pathway with TNF-R55-Ig did not affect the splenic architecture or the anti-SRBC response. Splenic defects and impaired **antibody** responses are seen in TNF-deficient mice, suggesting that TNF is important during development. Therefore relative to TNF, the LT system has the dominant influence on splenic organization and anti-SRBC Ig formation in the adult mouse.

L28 ANSWER 24 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 29 Mar 1997
ACCESSION NUMBER: 1997:205227 CAPLUS
DOCUMENT NUMBER: 126:198559
TITLE: Soluble **lymphotoxin**-β **receptors** and anti-lymphotoxin receptor and ligand **antibodies**, as

therapeutic agents for the **treatment** of immunological disease

INVENTOR(S): Browning, Jeffrey L.; Benjamin, Christopher D.; Hochman, Paula S.

PATENT ASSIGNEE(S): Biogen, Inc., USA; Browning, Jeffrey L.; Benjamin, Christopher D.; Hochman, Paula S.

SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9703687	A1	19970206	WO 1996-US12010	19960719
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
US 5925351	A	19990720	US 1995-505606	19950721
CA 2227477	AA	19970206	CA 1996-2227477	19960719
AU 9665912	A1	19970218	AU 1996-65912	19960719
AU 715407	B2	20000203		
EP 840616	A1	19980513	EP 1996-925393	19960719
EP 840616	B1	20041013		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
CN 1195294	A	19981007	CN 1996-196770	19960719
BR 9609716	A	19990706	BR 1996-9716	19960719
JP 11510488	T2	19990914	JP 1996-506919	19960719
NZ 313441	A	20000728	NZ 1996-313441	19960719
NZ 503818	A	20010831	NZ 1996-503818	19960719
PL 186911	B1	20040331	PL 1996-324622	19960719
AT 279205	E	20041015	AT 1996-925393	19960719
EP 1488799	A2	20041222	EP 2004-17208	19960719
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
PT 840616	T	20041231	PT 1996-925393	19960719
EE 4419	B1	20050215	EE 1998-13	19960719
ES 2225889	T3	20050316	ES 1996-925393	19960719
NO 9800172	A	19980323	NO 1998-172	19980114
FI 9800122	A	19980319	FI 1998-122	19980120
BG 63330	B1	20011031	BG 1998-102265	19980220
US 6403087	B1	20020611	US 1998-166	19980608
HK 1010832	A1	20050527	HK 1998-111990	19981113
US 6669941	B1	20031230	US 1999-303262	19990430
AU 748656	B2	20020606	AU 2000-27793	20000414
US 2005037003	A1	20050217	US 2002-77406	20020215

PRIORITY APPLN. INFO.:

US 1995-505606	A	19950721
EP 1996-925393	A3	19960719
NZ 1996-313441	A1	19960719
WO 1996-US12010	W	19960719

Searcher : Shears 571-272-2528

US 1998-166 A3 19980608

AB This invention relates to compns. and methods comprising " **lymphotoxin**-β **receptor** blocking agents", which block **lymphotoxin**-β **receptor** signalling. **Lymphotoxin**-β **receptor** blocking agents are useful for **treating** lymphocyte-mediated immunol. diseases, and more particularly, for inhibiting Th1 cell-mediated immune responses, e.g. delayed type hypersensitivity, contact hypersensitivity, tuberculin-type hypersensitivity, granulomatous, organ transplant rejection, and others. This invention also relates to the use of **antibodies** directed against either the **lymphotoxin**-β **receptor** or its ligand, surface lymphotoxin, that act as **lymphotoxin**-β **receptor** blocking agents. A novel screening method for selecting soluble receptors, **antibodies** and other agents that block **LT**-. **beta. receptor** signalling is provided.

L28 ANSWER 25 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 27 Mar 1997
ACCESSION NUMBER: 1997:199707 CAPLUS
DOCUMENT NUMBER: 126:276139
TITLE: Lymphotoxin-β receptor signaling complex: role of tumor necrosis factor receptor-associated factor 3 recruitment in cell death and activation of nuclear factor κB
AUTHOR(S): VanArsdale, Todd L.; VanArsdale, Sammee L.; Force, Walker R.; Walter, Barbara N.; Mosialos, George; Kieff, Elliott; Reed, John C.; Ware, Carl F.
CORPORATE SOURCE: Division of Biomedical Sciences, University of California, Riverside, CA, 92521, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1997), 94(6), 2460-2465
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The binding of heterotrimeric lymphotoxin, LTα1β2, to the **LTβ receptor** (**LT. beta.R**), a member of the tumor necrosis factor receptor (TNFR) superfamily, induces nuclear factor κB (NF-κB) activation and cell death in HT29 adenocarcinoma cells. The authors now show that **treatment** with LTα1β2 or agonistic **LT.beta.R** **antibodies** causes rapid recruitment of TNFR-associated factor 3 (TRAF3) to the **LT.beta.R** cytoplasmic domain. Further, stable overexpression of a TRAF3 mutant that lacks the RING and zinc finger domains inhibits **LTβ R**-mediated cell death. The inhibition is specific for **LT.beta.R** cell death signaling, since NF-κB activation by LTα1β2 and Fas-mediated apoptosis are not inhibited in the same cells. The mutant and endogenous TRAF3s are both recruited at equimolar amts. to the **LT.beta .R**, suggesting that the mutant disrupts the function of the signaling complex. These results implicate TRAF3 as a critical component of the **LT.beta.R** death signaling complex and indicate that at least 2 independent signaling pathways are

initiated by **LT.beta.R** ligation.
REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 26 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 15 Feb 1997
ACCESSION NUMBER: 1997:107934 CAPLUS
DOCUMENT NUMBER: 126:185005
TITLE: Fas involvement in human NK cell apoptosis: lack of a requirement for CD16-mediated events
AUTHOR(S): Ortaldo, John R.; Winkler-Pickett, Robin T.; Nagata, Shigekazu; Ware, Carl F.
CORPORATE SOURCE: National Cancer Inst., Frederick Cancer Res. and Development Center, Frederick, MD, USA
SOURCE: Journal of Leukocyte Biology (1997), 61(2), 209-215
CODEN: JLBIE7; ISSN: 0741-5400
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Propriocidal regulation of T cells refers to apoptosis induced by interleukin-2 (IL-2) activation with subsequent antigen receptor stimulation. We previously reported that natural killer (NK) cells also exhibit propriocidal death. Cell death can be induced following occupancy of the FcγRIII (CD16) receptor when NK cells were pretreated with IL-2, IL-12, or IL-15. Here we show other triggering receptors on NK cells such as CD44, anti-NK-receptor **antibodies**, and pharmacol. activation can result in the cell death signal. Requirement for cell interactions indicated that cell contact was required; however, unlike cell-mediated lysis, extracellular calcium was not required. Like T cells, the process of cell death for NK cells was receptor-induced apoptosis. Activation-induced apoptosis of T cells is mediated by members of the tumor necrosis factor (TNF) cytokine superfamily. We examined the involvement of TNF receptor family members or Fas in this rapid cell death. **Antibody** directed against Fas, TNFR60, TNFR80, **LTBR**, and LTα failed to inhibit receptor-induced death. Therefore, NK cells appear to demonstrate a rapid apoptotic episode when CD16 is cross-linked, but the mechanism of this apoptosis is quite different than was observed in T cells with CD3. The direct examination of the Fas pathway on activated NK cells revealed that susceptibility required longer **treatment** times and IL-2 activation. This susceptibility was paralleled by increased Fas-ligand expression. Therefore, NK cells can demonstrate an apoptotic response to CD16, CD44, NK receptors, and Fas. The enumeration of ligands capable of eliciting NK cell death and the in vivo relevance of this observation require further study.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 27 OF 27 CAPLUS COPYRIGHT 2005 ACS on STN
ED Entered STN: 03 Apr 1996
ACCESSION NUMBER: 1996:189896 CAPLUS
DOCUMENT NUMBER: 124:229647
TITLE: Signaling through the lymphotoxin β receptor

induces the death of some adenocarcinoma tumor lines

AUTHOR(S): Browning, Jeffrey L.; Miatkowski, Konrad; Sizing, Irene; Griffiths, David; Zafari, Mohammad; Benjamin, Christopher D.; Meier, Werner; Mackay, Fabienne

CORPORATE SOURCE: Dep. Immunol. Inflammation Protein Eng., Biogen, Cambridge, MA, 02142, USA

SOURCE: Journal of Experimental Medicine (1996), 183(3), 867-78
CODEN: JEMEAV; ISSN: 0022-1007

PUBLISHER: Rockefeller University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Surface lymphotoxin (LT) is a heteromeric complex of LT-α and LT-β chains that binds to the **LT-β receptor** (**LT-β -R**), a member of the tumor necrosis factor (TNF) family of receptors. The biol. function of this receptor-ligand system is poorly characterized. Since signaling through other members of this receptor family can induce cell death, e.g., the TNF and Fas receptors, it is important to determine if similar signaling events can be communicated via the **LT-β -R**. A soluble form of the surface complex was produced by coexpression of LT-α and a converted form of LT-β wherein the normally type II LT-β membrane protein was changed to a type I secreted form. Recombinant LT-α1/β2 was cytotoxic to the human adenocarcinoma cell lines HT-29, WiDr, MDA-MB-468, and HT-3 when added with the synergizing agent interferon (IFN) γ. When immobilized on a plastic surface, anti-**LT-β -R** monoclonal **antibodies** (mAbs) induced the death of these cells, demonstrating direct signaling via the **LT-beta.-R**. Anti-**LT-β -R** mAbs were also identified that inhibited ligand-induced cell death, whereas others were found to potentiate the activity of the ligand when added in solns. The human WiDr adenocarcinoma line forms solid tumors in immunocompromised mice, and **treatment** with an anti-**LT-β -R antibody** combined with human IFN-γ arrested tumor growth. The delineation of a biol. signaling event mediated by the **LT-beta.-R** opens a window for further studies on its immunol. role, and furthermore, activation of the **LT-beta.-R** may have an application in tumor **therapy**.

FILE 'SCISEARCH' ENTERED AT 12:10:54 ON 23 SEP 2005

FILE 'JICST-EPLUS' ENTERED AT 12:10:54 ON 23 SEP 2005

FILE 'JAPIO' ENTERED AT 12:10:54 ON 23 SEP 2005

FILE 'TOXCENTER' ENTERED AT 12:10:54 ON 23 SEP 2005

L30 89 S L28
L31 44 DUP REM L30 (45 DUPLICATES REMOVED)

L31 ANSWER 1 OF 44 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:180460 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA14304058519P
TITLE: Antibodies that specifically bind to TL5, a member of the TNF ligand superfamily, sequences thereof, and therapeutic and diagnostic uses
AUTHOR(S): Rosen, Craig A.; Ruben, Steven M.
CORPORATE SOURCE: ASSIGNEE: Human Genome Sciences, Inc.
PATENT INFORMATION: US 2005129614 A1 16 Jun 2005
SOURCE: (2005) U.S. Pat. Appl. Publ., 78 pp., Cont.-in-part of Appl. No. PCT/US03/10956.
CODEN: USXXCO.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2005:524968
LANGUAGE: English
ENTRY DATE: Entered STN: 20050705
Last Updated on STN: 20050719

AB The present invention relates to **antibodies** and related mols. (e.g. scFv, monoclonal **antibody**, chimeric **antibodies**, or fragments) that specifically bind to TL5, a member of the TNF (tumor necrosis factor) ligand superfamily. In specific embodiments, the **antibodies** of the invention inhibit TL5 binding to a TL5 receptor (e.g., TNF receptors TR2, TR6, or **LT.beta.R**). Such **antibodies** have uses, for example, in the **prevention** and **treatment** of cancer as well as immune system diseases and disorders including autoimmune disease, rheumatoid arthritis, graft rejection, graft vs. host disease, and lymphadenopathy. The invention also relates to nucleic acid mols. encoding anti-TL5 **antibodies**, vectors and host cells containing these nucleic acids, and methods for producing the same. The present invention relates to methods and compns. for **preventing**, detecting, diagnosing, **treating** or ameliorating a disorder, especially cancer as well as immune disorders, comprising administering to an animal, preferably a human, an effective amount of one or more **antibodies** that specifically bind to TL5.

L31 ANSWER 2 OF 44 JICST-EPlus COPYRIGHT 2005 JST on STN DUPLICATE 1
ACCESSION NUMBER: 1050225960 JICST-EPlus
TITLE: Role of Gut-Associated Lymphoreticular Tissues in Intestinal IgA Immunity

Searcher : Shears 571-272-2528

AUTHOR: YAMAMOTO M
CORPORATE SOURCE: Nihon Univ. School Of Dentistry At Matsudo, Chiba, Jpn
SOURCE: J Oral Biosci, (2005) vol. 47, no. 1, pp. 6-10. Journal Code: Y0018A (Fig. 2, Tbl. 1, Ref. 26)
ISSN: 1349-0079
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
STATUS: New

AB Despite the fact that intestinal IgA responses are known to be regulated by gut-associated lymphoreticular tissues (GALT), the exact sites where this regulatory network is formed are only partially understood. Our study shows that antigen-specific intestinal IgA **antibodies** are induced after oral immunization in mice made deficient in Peyer's patches (PP) by in utero **treatment** with **lymphotoxin**-B **receptor** and Ig (**LT.BETA.R**-Ig). These results suggest that the PP-independent pathways exist for antigen-specific intestinal IgA responses. On the other hand, postnatal **LT**B **R**-Ig-**treated** mice lacking isolated lymphoid follicles (ILF) were still able to produce significant mucosal IgA responses. Furthermore, mice **treated** with both TNF receptor p55 and Ig (TNFR55-Ig) and **LT.BETA.R**-Ig in utero, which lack PP and mesenteric lymph nodes (MLN) but retain intact ILF, failed to induce antigen-specific IgA responses after oral immunization. These findings demonstrated that ILF were not essential for induction of intestinal IgA responses. Interestingly, however, the IgA responses induced in the PP- or ILF-null mice were significantly lower than those seen in the control mice. Taken together, these findings suggest that aggregated lymphoid follicles residing in the intestinal lumen, e.g. PP and ILF, and draining MLN, may comprise an integrated regulatory network for the induction of maximum IgA **antibody** responses to orally administered antigens. (author abst.)

L31 ANSWER 3 OF 44 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
DUPLICATE 2
ACCESSION NUMBER: 2004-525790 [50] WPIDS
DOC. NO. CPI: C2004-193463
TITLE: New multivalent **antibody** constructs specific for the human **lymphotoxin-beta receptor**, useful for diagnosing or **treating** cancer or for inhibiting tumor volume.
DERWENT CLASS: B04 D16
INVENTOR(S): BAILLY, V; BROWNING, J L; GARBER, E
PATENT ASSIGNEE(S): (BIOG-N) BIOGEN IDEC MA INC
COUNTRY COUNT: 107
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004058191	A2	20040715	(200450)*	EN	85

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT

TZ UA UG US UZ VC VN YU ZA ZM ZW
AU 2003299984 A1 20040722 (200476)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004058191	A2	WO 2003-US41393	20031222
AU 2003299984	A1	AU 2003-299984	20031222

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003299984	A1 Based on	WO 2004058191

PRIORITY APPLN. INFO: US 2002-435154P 20021220
AN 2004-525790 [50] WPIDS
AB WO2004058191 A UPAB: 20040805
NOVELTY - A multivalent **antibody** comprising at least one antigen recognition site specific for a **lymphotoxin-beta receptor** (**LT- beta -R**) epitope, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a pharmaceutical composition comprising an amount of the multivalent **antibody** construct and a pharmaceutical carrier;
(2) a method of **treating** cancer in a subject, comprising administering to the subject an amount of the above composition to the subject;
(3) a nucleic acid comprising any of the 5 sequences having 645-2208 bp fully defined in the specification (SEQ ID NO: 1, 3, 5, 7 or 9);
(4) a polypeptide comprising any of the 5 sequences having 194-735 amino acids fully defined in the specification (SEQ ID NO: 2, 4, 6, 8 or 10);
(5) an expression vector comprising the above nucleic acid; and
(6) a cell comprising the expression vector.
ACTIVITY - Cytostatic.
No biological data given.
MECHANISM OF ACTION - None given.
No biological data given.
USE - The **antibody** is useful for preparing a medicament for the **treatment** of cancer (claimed). The composition and method are used for diagnosing or **treating** cancer and for inhibiting tumor volume.
Dwg.0/11

L31 ANSWER 4 OF 44 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
DUPLICATE 3
ACCESSION NUMBER: 2004-376051 [35] WPIDS
DOC. NO. CPI: C2004-141433
TITLE: Treating an animal having an immunological renal disorder or glomerulonephritis comprises administering to the mammal a composition comprising an inhibitor of the lymphotoxin (LT) pathway.
DERWENT CLASS: B04 D16
INVENTOR(S): BROWNING, J L; GOMMERMAN, J
PATENT ASSIGNEE(S): (BIOJ) BIOGEN INC; (BIOJ) BIOGEN IDEC MA INC

COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004039329	A2	20040513	(200435)*	EN	47
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
AU 2003287431	A1	20040525	(200468)		
EP 1565214	A2	20050824	(200556)	EN	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004039329	A2	WO 2003-US34813	20031031
AU 2003287431	A1	AU 2003-287431	20031031
EP 1565214	A2	EP 2003-781666	20031031
		WO 2003-US34813	20031031

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003287431	A1 Based on	WO 2004039329
EP 1565214	A2 Based on	WO 2004039329

PRIORITY APPLN. INFO: US 2002-422588P 20021031
AN 2004-376051 [35] WPIDS
AB WO2004039329 A UPAB: 20040603

NOVELTY - Treating an animal having an immunological renal disorder or glomerulonephritis comprises administering to the mammal a composition comprising an inhibitor of the lymphotoxin (LT) pathway.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a method for evaluating the efficacy of a compound for treating IgA nephropathy comprising:

(a) administering the compound to a BAFF-transgenic animal;

(b) determining the test level of IgA deposits in a kidney of the animal after administration; and

(c) comparing the level with a threshold level, where a test level lower than the threshold level indicates that the compound is efficacious.

ACTIVITY - Endocrine-Gen; Antiinflammatory.

No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The method and composition are useful for treating an immunological renal disorder, e.g. systemic lupus erythematosus, Sjorgen's syndrome, rheumatoid arthritis, insulin-dependent diabetes mellitus, chronic hepatitis, Henoch-Schonlein purpura, and IgA nephropathy, or glomerulonephritis.

Dwg.0/7

L31 ANSWER 5 OF 44 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
DUPLICATE 4
ACCESSION NUMBER: 2004-082874 [08] WPIDS
DOC. NO. CPI: C2004-034090
TITLE: New humanized anti-**lymphotoxin-beta receptor antibodies** having light and heavy chain complementary determining regions, useful for **treating** or reducing cancers and/or solid tumors, including lung, breast and prostate cancers.
DERWENT CLASS: B04 D16
INVENTOR(S): GARBER, E; SALDANHA, J; SIMON, K
PATENT ASSIGNEE(S): (BIOJ) BIOGEN INC
COUNTRY COUNT: 106
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004002431	A2	20040108	(200408)*	EN	82
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
AU 2003248782	A1	20040119	(200447)		
EP 1539793	A2	20050615	(200539)	EN	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004002431	A2	WO 2003-US20762	20030701
AU 2003248782	A1	AU 2003-248782	20030701
EP 1539793	A2	EP 2003-762296	20030701
		WO 2003-US20762	20030701

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003248782	A1 Based on	WO 2004002431
EP 1539793	A2 Based on	WO 2004002431

PRIORITY APPLN. INFO: US 2002-417372P 20021009; US 2002-392993P 20020701
AN 2004-082874 [08] WPIDS
AB WO2004002431 A UPAB: 20040202
NOVELTY - A humanized anti-**lymphotoxin-beta receptor** (**LT- beta -R**) **antibody** comprising light chain complementary determining regions defined by residues 24-34, 50-56 and 89-97 of a 107 amino acid sequence (SEQ ID NO: 1), and heavy chain complementary determining regions defined by residues 31-35, 50-65 and 95-102 of a 116 amino acid sequence (SEQ ID NO: 2), both given in the specification, is new.
DETAILED DESCRIPTION - A humanized anti-**lymphotoxin**-

beta receptor (**LT- beta -R**) **antibody** comprising light chain complementary determining regions defined by residues 24-34, 50-56 and 89-97 of a 107 amino acid sequence (SEQ ID NO: 1), and heavy chain complementary determining regions defined by residues 31-35, 50-65 and 95-102 of a 116 amino acid sequence (SEQ ID NO: 2), both given in the specification, is new. The **LT- beta -R antibody** further comprises at least one of residues Y36, S49, T63 and F87 in its light chain, or at least one of residues Y27, T30,148, A67, L69 and F91 (Kabat numbering convention) in its heavy chain.

INDEPENDENT CLAIMS are also included for the following:

(1) an **antibody** that binds to the same epitope of **lymphotoxin-beta receptor** as the humanized **antibody** cited above;

(2) a humanized anti-**lymphotoxin-beta receptor** (**LT- beta -R**) **antibody** whose light chain complementary determining regions are defined by residues 24-34, 50-56 and 89-97 of SEQ ID NO: 1, and whose heavy chain complementary determining regions are defined by residues 31-35, 50-65 and 95-102 of SEQ ID NO: 2, and wherein the **antibody** comprises residue Y36, S49 and F87 in its light chain (Kabat numbering convention);

(3) a humanized anti-**lymphotoxin-beta receptor** (**LT- beta -R**) **antibody** whose light chain complementary determining regions are defined by residues 24-34, 50-56 and 89-97 of SEQ ID NO:1, and whose heavy chain complementary determining regions are defined by residues 31-35, 50-65 and 95-102 of SEQ ID NO: 2, and wherein the **antibody** comprises residue Y27 and T30 in its heavy chain (Kabat numbering convention);

(4) an **antibody** comprising the same heavy and light chain polypeptide sequences as an **antibody** produced by cell line Clone 3D9 with ATCC patent deposit designation PTA-4726, deposited on September 27, 2002;

(5) a cell producing any of the **antibodies**;

(6) a composition comprising any of the **antibodies** and a carrier;

(7) **treating** or reducing the advancement, severity or effects of neoplasia in a human, comprising administering the composition of (6) to the human;

(8) reducing tumor volume in a human, comprising administering the composition of (6) to the human;

(9) an isolated nucleic acid comprising a coding sequence for the light or heavy chain of the **antibody** of (4);

(10) an isolated nucleic acid comprising a coding sequence for residues 1-107 of a 321 amino acid sequence (SEQ ID NO: 5) or residues 1-113 of a 348 amino acid sequence (SEQ ID NO: 13), both given in the specification;

(11) an expression vector comprising the nucleic acid of (10);

(12) a cell comprising the expression vector of (11);

(13) a cell of cell line Clone 3D9 with ATCC patent deposit designation PTA-4726, deposited on September 27, 2002;

(14) an **antibody** or antigen-binding fragment of any of the **antibodies**, wherein the **antibody** is conjugated to polyethylene glycol or albumen, and wherein the constant region of the **antibody** is modified to reduce at least one constant region-mediated biological effector function relative to an unmodified **antibody**, and comprising an Fc region having an altered

effector function;
(15) a hybridoma cell consisting of 3D9 with ATCC Accession Number PTA-4726;
(16) a light chain comprising the complementarity determining regions (CDRs) and variable region framework amino acid residues Y36, S49, and F87 (Kabat numbering system) from SEQ ID NO: 1, wherein the remainder of the light chain is from a human **antibody**;
(17) a heavy chain comprising the complementarity determining regions (CDRs) and variable region framework amino acid residues Y27 and T30 (Kabat numbering system) from SEQ ID NO: 2, wherein the remainder of the heavy chain is from a human **antibody**;
(18) a humanized **antibody** comprising the light chain of (16), and the heavy chain of (17), or antigen-binding fragments of the **antibody**;
(19) a humanized **antibody** comprising the CDRs of the BHA10 variable light chain sequence with SEQ ID NO: 1, or the CDRs of the BHA10 variable heavy chain sequence with forth as SEQ ID NO: 2;
(20) a humanized **antibody**, or its antigen-binding fragment, which specifically binds **LT- beta - R**, comprising a variable region comprising CDRs corresponding to CDRs from the mouse BHA10 **antibody**;
(21) **treating** or reducing cancer in a patient, comprising administering to the patient a humanized **antibody** of (18)-(20); and
(22) **treating** or reducing a solid tumor in a patient, comprising administering to the patient a humanized **antibody** of (18)-(20).
ACTIVITY - Cytostatic.
No biological data is given.
MECHANISM OF ACTION - Lympthoxin-Antagonist-Beta.
USE - The methods and compositions of the present invention are useful for **treating** or reducing cancers or solid tumors, including non small cell lung cancer (NSCLC), colorectal cancer (CRC), breast cancer, prostate cancer, gastric cancer, skin cancer, stomach cancer, esophagus cancer, and bladder cancer (claimed).
Dwg.0/6

L31 ANSWER 6 OF 44 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-525785 [50] WPIDS
DOC. NO. CPI: C2004-193458
TITLE: Inhibiting tumor volume comprising administering an amount of a lymphotoxin-beta receptor agonist or antibody and a chemotherapeutic agent (e.g. gemcitabine or adriamycin).
DERWENT CLASS: B04 B05 D16
INVENTOR(S): GILL, A; LEPAGE, D
PATENT ASSIGNEE(S): (BIOG-N) BIOGEN IDEC MA INC
COUNTRY COUNT: 107
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004058183	A2	20040715	(200450)*	EN	161

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT

TZ UA UG US UZ VC VN YU ZA ZM ZW
AU 2003303339 A1 20040722 (200476)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004058183	A2	WO 2003-US41243	20031222
AU 2003303339	A1	AU 2003-303339	20031222

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003303339	A1 Based on	WO 2004058183

PRIORITY APPLN. INFO: US 2002-435185P 20021220
AN 2004-525785 [50] WPIDS
AB WO2004058183 A UPAB: 20040805
NOVELTY - Inhibiting tumor volume comprises administering an amount of a **lymphotoxin-beta receptor** (**LT - beta -R**) agonist or **antibody** and an amount of at least one chemotherapeutic agent, where the administration of the **LT- beta -R** agonist or **antibody** and the chemotherapeutic agent results in supra-additive inhibition of the tumor.

DETAILED DESCRIPTION - AN INDEPENDENT CLAIM is also included for the pharmaceutical composition comprising an amount of an **LT - beta -R** agonist and at least one chemotherapeutic agent, and a pharmaceutical carrier, which upon administration to a subject results in supra-additive inhibition of a tumor.

ACTIVITY - Cytostatic.
No biological data given.
MECHANISM OF ACTION - Gene **therapy**.
USE - The method is useful for inhibiting tumor volume or for **treating** cancer. The **lymphotoxin-beta receptor** agonist and the chemotherapeutic agent are useful for preparing a medicament for the **treatment** of cancer, which upon administration to a subject results in supra-additive inhibition of a tumor (claimed).
Dwg.0/15

L31 ANSWER 7 OF 44 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-376164 [35] WPIDS
DOC. NO. CPI: C2004-141493
TITLE: New trimeric binding polypeptides for trimeric cytokines, useful for preparing a pharmaceutical composition for the treatment of pathologies mediated by trimeric cytokines, e.g. rheumatoid arthritis, psoriasis or Crohn's disease.
DERWENT CLASS: B04 D16
INVENTOR(S): ANDERSEN, M H; HOLTET, T L; OTTOW, H K
PATENT ASSIGNEE(S): (BORE-N) BOREAN PHARMA AS; (OTTO-I) OTTOW H K
COUNTRY COUNT: 106
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

WO 2004039841 A2 20040513 (200435)* EN 96
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
AU 2003277828 A1 20040525 (200468)
EP 1558640 A2 20050803 (200551) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004039841	A2	WO 2003-DK735	20031029
AU 2003277828	A1	AU 2003-277828	20031029
EP 1558640	A2	EP 2003-769251	20031029
		WO 2003-DK735	20031029

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003277828	A1 Based on	WO 2004039841
EP 1558640	A2 Based on	WO 2004039841

PRIORITY APPLN. INFO: US 2002-421807P 20021029; DK 2002-1634 20021029

AN 2004-376164 [35] WPIDS

AB WO2004039841 A UPAB: 20040603

NOVELTY - A trimeric polypeptide comprising three monomers, each of the monomers comprising a specific binding member capable of binding a trimeric cytokine, and each of the monomers comprising a trimerizing domain, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a pharmaceutical composition comprising the above trimeric polypeptide;

(2) a method of treating a subject having a pathology mediated by a trimeric cytokine such as a tumor necrosis factor, comprising administering to the subject an amount of the above trimeric polypeptide or composition;

(3) a method of preparing the trimeric polypeptide cited above, comprising culturing a host transformed with a vector encoding the trimeric polypeptide under such conditions that the trimeric polypeptide is expressed, and isolating the trimeric polypeptide; and

(4) an assay method for detecting a trimeric cytokine in a sample, comprising contacting the sample with the above trimeric polypeptide, and detecting the binding of the trimeric polypeptide to the trimeric cytokine.

ACTIVITY - Antirheumatic; Antiarthritic; Antipsoriatic; Anti-inflammatory; Antimicrobial; Cytostatic; Neuroprotective.

No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The trimeric polypeptide is useful for preparing a pharmaceutical composition (claimed) that may be used for treating a pathology mediated by a trimeric cytokine, such as rheumatoid

organization and antiSRBC Ig formation in the adult mouse.

L31 ANSWER 40 OF 44 MEDLINE on STN DUPLICATE 19
ACCESSION NUMBER: 97174193 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9021927
TITLE: Fas involvement in human NK cell apoptosis: lack of a requirement for CD16-mediated events.
AUTHOR: Ortaldo J R; Winkler-Pickett R T; Nagata S; Ware C F
CORPORATE SOURCE: Division of Basic Sciences, National Cancer Institute, Frederick Cancer Research and Development Center, Maryland 21702-1201, USA.
SOURCE: Journal of leukocyte biology, (1997 Feb) 61 (2) 209-15. Journal code: 8405628. ISSN: 0741-5400.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970306
Last Updated on STN: 19970306
Entered Medline: 19970226

AB Propriocidal regulation of T cells refers to apoptosis induced by interleukin-2 (IL-2) activation with subsequent antigen receptor stimulation. We previously reported that natural killer (NK) cells also exhibit propriocidal death. Cell death can be induced following occupancy of the Fc gamma RIII (CD16) receptor when NK cells were pretreated with IL-2, IL-12, or IL-15. Here we show other triggering receptors on NK cells such as CD44, anti-NK-receptor **antibodies**, and pharmacological activation can result in the cell death signal. Requirement for cell interactions indicated that cell contact was required; however, unlike cell-mediated lysis, extracellular calcium was not required. Like T cells, the process of cell death for NK cells was receptor-induced apoptosis. Activation-induced apoptosis of T cells is mediated by members of the tumor necrosis factor (TNF) cytokine superfamily. We examined the involvement of TNF receptor family members or Fas in this rapid cell death. **Antibody** directed against Fas, TNFR60, TNFR80, **LTBR**, and LT alpha failed to inhibit receptor-induced death. Therefore, NK cells appear to demonstrate a rapid apoptotic episode when CD16 is cross-linked, but the mechanism of this apoptosis is quite different than was observed in T cells with CD3. The direct examination of the Fas pathway on activated NK cells revealed that susceptibility required longer **treatment** times and IL-2 activation. This susceptibility was paralleled by increased Fas-ligand expression. Therefore, NK cells can demonstrate an apoptotic response to CD16, CD44, NK receptors, and Fas. The enumeration of ligands capable of eliciting NK cell death and the in vivo relevance of this observation require further study.

L31 ANSWER 41 OF 44 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 1996-362460 [36] WPIDS
DOC. NO. NON-CPI: N1996-305569
DOC. NO. CPI: C1996-114130
TITLE: Treatment of neoplasia by killing tumour cells - using a lymphotoxin alpha/beta hetero-dimeric complex or a lymphotoxin-beta receptor activating agent.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): BENJAMIN, C D; BROWNING, J L; MEIER, W; BENJAMIN, D; BROWNING, L

PATENT ASSIGNEE(S): (BIOJ) BIOGEN INC; (BIOJ) BIOGEN IDEC MA INC; (BENJ-I) BENJAMIN C D; (BROW-I) BROWNING J L; (MEIE-I) MEIER W
COUNTRY COUNT: 71
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9622788	A1	19960801	(199636)*	EN	76
RW: AT BE CH DE DK EA ES FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG					
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN					
AU 9649704	A	19960814	(199650)		
NO 9703385	A	19970925	(199749)		
FI 9703118	A	19970925	(199751)		
EP 809510	A1	19971203	(199802)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE SI					
BR 9606808	A	19971230	(199807)		
CZ 9702361	A3	19980218	(199813)		
MX 9705629	A1	19971001	(199901)		
HU 9801746	A2	19981130	(199903)		
JP 10513161	W	19981215	(199909)		61
KR 98701816	A	19980625	(199924)		
NZ 303405	A	20000228	(200017)		
SK 9700986	A3	20000214	(200020)		
AU 725351	B	20001012	(200055)		
US 6312691	B1	20011106	(200170)		
CN 1177302	A	19980325	(200209)		
US 2002090366	A1	20020711	(200248)		
RO 118634	B1	20030829	(200374)		
EP 1407781	A1	20040414	(200426)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE					
EP 809510	B1	20040609	(200438)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE SI					
DE 69632681	E	20040715	(200446)		
ES 2220972	T3	20041216	(200506)		
KR 2004102364	A	20041204	(200525)		
DE 69632681	T2	20050609	(200538)		
CN 1589902	A	20050309	(200542)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9622788	A1	WO 1996-US1386	19960126
AU 9649704	A	AU 1996-49704	19960126
		WO 1996-US1386	19960126
NO 9703385	A	WO 1996-US1386	19960126
		NO 1997-3385	19970722
FI 9703118	A	WO 1996-US1386	19960126
		FI 1997-3118	19970725
EP 809510	A1	EP 1996-906260	19960126
		WO 1996-US1386	19960126
BR 9606808	A	BR 1996-6808	19960126
		WO 1996-US1386	19960126
CZ 9702361	A3	WO 1996-US1386	19960126
		CZ 1997-2361	19960126

Searcher : Shears 571-272-2528

MX 9705629	A1		MX 1997-5629	19970725
HU 9801746	A2		WO 1996-US1386	19960126
			HU 1998-1746	19960126
JP 10513161	W		JP 1996-523078	19960126
			WO 1996-US1386	19960126
KR 98701816	A		WO 1996-US1386	19960126
			KR 1997-705213	19970726
NZ 303405	A		NZ 1996-303405	19960126
			WO 1996-US1386	19960126
SK 9700986	A3		WO 1996-US1386	19960126
			SK 1997-986	19960126
AU 725351	B		AU 1996-49704	19960126
US 6312691	B1		WO 1996-US1386	19960126
			US 1998-875560	19980605
CN 1177302	A		CN 1996-192271	19960126
US 2002090366	A1	CIP of	US 1995-378968	19950126
		Div ex	WO 1996-US1386	19960126
		Div ex	US 1998-875560	19980605
			US 2001-931402	20010816
RO 118634	B1		WO 1996-US1386	19960126
			RO 1997-1398	19960126
EP 1407781	A1	Div ex	EP 1996-906260	19960126
			EP 2003-22584	19960126
EP 809510	B1		EP 1996-906260	19960126
			WO 1996-US1386	19960126
		Related to	EP 2003-22584	19960126
DE 69632681	E		DE 1996-632681	19960126
			EP 1996-906260	19960126
			WO 1996-US1386	19960126
ES 2220972	T3		EP 1996-906260	19960126
KR 2004102364	A		KR 2004-715796	20041004
DE 69632681	T2		DE 1996-632681	19960126
			EP 1996-906260	19960126
			WO 1996-US1386	19960126
CN 1589902	A	Div ex	CN 1996-192271	19960126
			CN 2004-7058	19960126

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9649704	A	Based on	WO 9622788
EP 809510	A1	Based on	WO 9622788
BR 9606808	A	Based on	WO 9622788
CZ 9702361	A3	Based on	WO 9622788
HU 9801746	A2	Based on	WO 9622788
JP 10513161	W	Based on	WO 9622788
KR 98701816	A	Based on	WO 9622788
NZ 303405	A	Based on	WO 9622788
AU 725351	B	Previous Publ.	AU 9649704
		Based on	WO 9622788
US 6312691	B1	Based on	WO 9622788
RO 118634	B1	Based on	WO 9622788
EP 1407781	A1	Div ex	EP 809510
EP 809510	B1	Related to	EP 1407781
		Based on	WO 9622788
DE 69632681	E	Based on	EP 809510
		Based on	WO 9622788
ES 2220972	T3	Based on	EP 809510

Searcher : Shears 571-272-2528

DE 69632681 T2 Based on EP 809510
Based on WO 9622788

PRIORITY APPLN. INFO: US 1995-378968 19950126; US
1998-875560 19980605; US
2001-931402 20010816

AN 1996-362460 [36] WPIDS

AB WO 9622788 A UPAB: 19960913

A method (A) for **treating** or reducing the advancement, severity or effects of neoplasia, comprises: administering: (i) a lymphotoxin (LT)-alpha/beta heteromeric complex (LHC) and a carrier, or (ii) 1 **LT-beta receptor** (**LT-beta-R**) activating agent and a carrier.

Also claimed are: (1) a method (B) for selecting a **LT-beta-R** activating agent which acts in the presence of a LHC, comprising: (a) culturing tumour cells in the presence of LHCs, a first **LT-beta-R** activating agent and a second putative **LT-beta-R** activating agent; and (b) determining whether the second putative **LT-beta-R** activating agent increases the anti-tumour activity of the LHC in the presence of the first **LT-beta-R** activating agent;

(2) a pharmaceutical compsn. comprising an LHC and a carrier;

(3) a pharmaceutical compsn. comprising 1 **LT-beta-R** activating agent without exogenous LHC and a carrier, and

(4) a pharmaceutical compsn. comprising cross-linked anti-**LT-beta-R antibodies** as a **LT-beta-R** activating agent and a carrier.

USE - The prods. and methods are used in the **treatment** of tumours.

ADVANTAGE - **Treatment** with LHC or **LT-beta-R** activating agents can induce cytotoxic effects in tumourigenic cells without the potent side effect problems encountered when tumour necrosis factor receptor (TNF-R) or Fas receptor (FasR) activation has been used as an anti-tumour **treatment**.

Dwg.0/6

L31 ANSWER 42 OF 44 MEDLINE on STN DUPLICATE 20
ACCESSION NUMBER: 96228308 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8642291
TITLE: Signaling through the lymphotoxin-beta receptor induces the death of some adenocarcinoma tumor lines.
AUTHOR: Browning J L; Miatkowski K; Sizing I; Griffiths D; Zafari M; Benjamin C D; Meier W; Mackay F
CORPORATE SOURCE: Department of Immunology and Inflammation, Biogen, Cambridge, Massachusetts 02142, USA.
SOURCE: Journal of experimental medicine, (1996 Mar 1) 183 (3) 867-78.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 19960726
Last Updated on STN: 19970203
Entered Medline: 19960716

Searcher : Shears 571-272-2528

AB Surface lymphotoxin (LT) is a heteromeric complex of LT-alpha and LT-beta chains that binds to the **LT-beta receptor** (**LT-beta-R**), a member of the tumor necrosis factor (TNF) family of receptors. The biological function of this receptor-ligand system is poorly characterized. Since signaling through other members of this receptor family can induce cell death, e.g., the TNF and Fas receptors, it is important to determine if similar signaling events can be communicated via the **LT-beta-R**. A soluble form of the surface complex was produced by coexpression of LT-alpha and a converted form of LT-beta wherein the normally type II LT-beta membrane protein was changed to a type I secreted form. Recombinant LT-alpha 1/beta 2 was cytotoxic to the human adenocarcinoma cell lines HT-29, WiDr, MDA-MB-468, and HT-3 when added with the synergizing agent interferon (IFN) gamma. When immobilized on a plastic surface, anti-**LT-beta-R** monoclonal **antibodies** (mAbs) induced the death of these cells, demonstrating direct signaling via the **LT-beta-R**. Anti-**LT-beta-R** mAbs were also identified that inhibited ligand-induced cell death, whereas others were found to potentiate the activity of the ligand when added in solution. The human WiDr adenocarcinoma line forms solid tumors in immunocompromised mice, and **treatment** with an anti-**LT-beta-R antibody** combined with human IFN-gamma arrested tumor growth. The delineation of a biological signaling event mediated by the **LT-beta-R** opens a window for further studies on its immunological role, and furthermore, activation of the **LT-beta-R** may have an application in tumor **therapy**.

L31 ANSWER 43 OF 44 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1996:351623 BIOSIS
DOCUMENT NUMBER: PREV199699073979
TITLE: Growth arrest of WiDr adenocarcinoma tumors in SCID mice following **treatment** with an anti-human **LT-beta-R** agonist **antibody** in combination with INF-gamma: A possible tumor differentiation process.
AUTHOR(S): Mackay, Fabienne; Browning, Jeffrey L.
CORPORATE SOURCE: Dep. Immunol. and Inflammation, Biogen Inc., Cambridge, MA, USA
SOURCE: European Cytokine Network, (1996) Vol. 7, No. 2, pp. 264.
Meeting Info.: 6th International Tumor Necrosis Factor Congress. Rhodes, Greece. May 8-12, 1996.
ISSN: 1148-5493.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Aug 1996
Last Updated on STN: 5 Aug 1996

L31 ANSWER 44 OF 44 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1996:283947 SCISEARCH
THE GENUINE ARTICLE: UE287
TITLE: Eosinophil chemotactic activity in bronchoalveolar lavage fluid obtained from Toxocara canis-infected

rats

AUTHOR: Okada K (Reprint); Fujimoto K; Kubo K; Sekiguchi M; Sugane K
CORPORATE SOURCE: SHINSHU UNIV, SCH MED, DEPT INTERNAL MED 1, 3-1-1 ASAHI, MATSUMOTO, NAGANO 390, JAPAN (Reprint); SHINSHU UNIV, SCH MED, DEPT PARASITOL, MATSUMOTO, NAGANO 390, JAPAN
COUNTRY OF AUTHOR: JAPAN
SOURCE: CLINICAL IMMUNOLOGY AND IMMUNOPATHOLOGY, (MAR 1996) Vol. 78, No. 3, pp. 256-262.
ISSN: 0090-1229.
PUBLISHER: ACADEMIC PRESS INC JNL-COMP SUBSCRIPTIONS, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 26
ENTRY DATE: Entered STN: 1996
Last Updated on STN: 1996
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We examined eosinophil chemotactic activity (EGA) in bronchoalveolar lavage fluid (BALF) obtained from rats infected with Toxocara canis. For 4 weeks after infection, the number of eosinophils was determined in peripheral blood and BALF. ECA was assayed using a microchemotaxis chamber. Eosinophils in peripheral blood and BALF increased markedly after infection, peaking at 12 days and 2 weeks, respectively. ECA in BALF also increased significantly and peaked 2 weeks after infection. Partial characterization revealed that ECA was heat labile, lipid soluble, and resistant to trypsin digestion. Two ECA peaks were identified by molecular sieve column chromatography: one near the egg albumin marker (MW 45,000) and the other observed after elution with quinacrine (MW 472.9). **Treatment** with a specific leukotriene (**LT**) **B** -4 **receptor** antagonist (ONO-4057), a platelet-activating factor (PAF) receptor antagonist (TCV-309), and an anti-interleukin (IL)-5 monoclonal **antibody** (TB13) significantly reduced the EGA, suggesting that LTB(4), PAF, and IL-5 contribute to the accumulation of eosinophils in the lungs of rats infected with T. canis. (C) 1996 Academic Press, Inc.

FILE 'MEDLINE' ENTERED AT 12:12:31 ON 23 SEP 2005

FILE LAST UPDATED: 22 SEP 2005 (20050922/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

Searcher : Shears 571-272-2528

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L33        2150 SEA FILE=MEDLINE ABB=ON  PLU=ON  LYMPHOTOXIN/CT
L34        3655 SEA FILE=MEDLINE ABB=ON  PLU=ON  "IMMUNOGLOBULINS, FC"/CT
L35       63785 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANTIBODIES/CT
L36         118 SEA FILE=MEDLINE ABB=ON  PLU=ON  L33 AND (L34 OR L35)
L37           9 SEA FILE=MEDLINE ABB=ON  PLU=ON  L36 AND (THERAPY OR
                  THERAPEUTIC USE)/CT
```

L37 ANSWER 1 OF 9 MEDLINE on STN
ACCESSION NUMBER: 78105854 MEDLINE
DOCUMENT NUMBER: PubMed ID: 304779
TITLE: Lymphocytotoxins in epileptic patients receiving phenytoin.
AUTHOR: Ooi B S; Kant K S; Hanenson I B; Pesce A J; Pollak V E
SOURCE: Clinical and experimental immunology, (1977 Oct) 30 (1) 56-61.
Journal code: 0057202. ISSN: 0009-9104.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197804
ENTRY DATE: Entered STN: 19900314
Last Updated on STN: 19900314
Entered Medline: 19780426

ED Entered STN: 19900314
Last Updated on STN: 19900314
Entered Medline: 19780426

AB The present study was undertaken to determine the prevalence and nature of lymphocytotoxic antibodies in patients receiving phenytoin. Of forty-six sera examined, lymphocytotoxins and antinuclear antibodies were detected in fourteen and eleven samples respectively. Antibodies to double-stranded RNA (poly-A-poly-U) were found in six out of thirty-eight sera studied. A highly significant correlation was found between the presence of lymphocytotoxins and antinuclear antibodies (chi2 = 9.72; P less than 0.01). Lymphocytotoxins were found to be of the IgM class, to have activity against T and B cells, and to be dependent on the presence of Ca and Mg ions for activity. These findings may have pathogenetic importance in the genesis of the altered immune state of patients reveiving phenytoin.

L37 ANSWER 2 OF 9 MEDLINE on STN
ACCESSION NUMBER: 77085889 MEDLINE
DOCUMENT NUMBER: PubMed ID: 64126
TITLE: [Immunologic abnormalities during treatment with penicillamine].
A propos d'anomalies immunologiques au cours de traitements par penicillamine.
AUTHOR: Recordier A M; Roux H; Mercier P; Maestracci D; Schiano A
SOURCE: Annales de medecine interne, (1976 AUG-SEP) 127 (8-9) 566-70.
Journal code: 0171744. ISSN: 0003-410X.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197702
ENTRY DATE: Entered STN: 19900313

Searcher : Shears 571-272-2528

Last Updated on STN: 19900313
Entered Medline: 19770216

ED Entered STN: 19900313
Last Updated on STN: 19900313
Entered Medline: 19770216

L37 ANSWER 3 OF 9 MEDLINE on STN
ACCESSION NUMBER: 76186646 MEDLINE
DOCUMENT NUMBER: PubMed ID: 131667
TITLE: Mixed leucocyte culture blocking factor activity in allograft recipients and its role in the clinical outcome of human cadaveric renal allografts.
AUTHOR: Sengar D P; Rashid A; Harris J E
SOURCE: Clinical and experimental immunology, (1975 Dec) 22 (3) 409-18.
Journal code: 0057202. ISSN: 0009-9104.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197608
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 19900313
Entered Medline: 19760803

ED Entered STN: 19900313
Last Updated on STN: 19900313
Entered Medline: 19760803

AB Seventeen renal allograft recipients were followed serially both pre- and post-transplantation for the presence of mixed leucocyte culture blocking factor activity (MLC-BFA) in their plasma. Patients could be divided into three distinct groups on the basis of MLC-BFA and lymphocytotoxin (LT) determinations. Fifteen out of seventeen patients possessed MLC-BFA at one time or another while four out of seventeen were positive for LT. Four patients of group 1 with pre-transplant LT and MLC-BFA rejected their grafts within 1 year. Two LT negative patients of group 2 developed no detectable MLC-BFA during a follow-up period of over 1 year. One other patient developed MLC-BFA 8 months following transplantation. All three patients had an excellent clinical course. Ten patients belonging to group 3 possessed no LT or MLC-BFA prior to transplantation but developed MLC-BFA alone after receiving an allograft. Only one patient rejected his allograft within 2 months. The remaining nine patients experienced mild rejection crises during the first 3 months after transplantation but had excellent renal function at 1 year or beyond that time. Our results indicate that MLC-BFA in the presence of LT may not prevent rejection. MLC-BFA is associated with a good clinical course in LT negative patients. However, certain patients who fail to develop LT or MLC-BFA in spite of repeated blood transfusions prior to transplantation may also do extremely well in the absence of detectible MLC-BFA.

L37 ANSWER 4 OF 9 MEDLINE on STN
ACCESSION NUMBER: 76092591 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1081959
TITLE: [Behavior of lymphocytotoxic antibodies during the chloroquine treatment of discoid lupus erythematosus]. Das Verhalten der lymphozytotoxischen Antikorper wahrend der Chlorochin-Behandlung des diskoiden Lupus erythematodes.

Searcher : Shears 571-272-2528

AUTHOR: Nagy E; Stenszky V; Szerze P
SOURCE: Dermatologische Monatschrift, (1975 Aug) 161 (8) 609-11.
Journal code: 0232053. ISSN: 0011-9083.
PUB. COUNTRY: GERMANY, EAST: German Democratic Republic
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197603
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 19900313
Entered Medline: 19760320
ED Entered STN: 19900313
Last Updated on STN: 19900313
Entered Medline: 19760320

L37 ANSWER 5 OF 9 MEDLINE on STN
ACCESSION NUMBER: 75160973 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4617974
TITLE: [Intermittent haemodialysis and HL-A antibody production before and after kidney transplantation (author's transl)].
Chronische dialyse und HL-A Antikorperbildung vor und nach Nierentransplantation.
AUTHOR: Speiser P; Mayr W R; Bleier I; Meizer G; Pacher M; Pausch V; Reiterer C; Weirather M
SOURCE: Wiener klinische Wochenschrift, (1974 Nov 29) 86 (22) 676-82.
Journal code: 21620870R. ISSN: 0043-5325.
PUB. COUNTRY: Austria
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197507
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19750724
ED Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19750724

L37 ANSWER 6 OF 9 MEDLINE on STN
ACCESSION NUMBER: 75083414 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4280561
TITLE: [Anti-HL-A antibodies not fixing complement (blocking)].
Anticorps anti-HL-A ne fixant pas le complement (bloquants).
AUTHOR: Colombani J; Colombani M; Lepage V
SOURCE: Nouvelle revue francaise d'hematologie, (1974 Jul-Aug) 14 (4) 518-30.
Journal code: 0401074. ISSN: 0029-4810.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197504
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19900310

Searcher : Shears 571-272-2528

Entered Medline: 19750423
ED Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19750423

L37 ANSWER 7 OF 9 MEDLINE on STN
ACCESSION NUMBER: 74262963 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4600511
TITLE: The effect of extracorporeal irradiation of the blood in necrokidney transplantation. Three years' follow-up study.
AUTHOR: Weeke E; Thaysen J H
SOURCE: Acta medica Scandinavica, (1974 Jun) 195 (6) 485-91.
Journal code: 0370330. ISSN: 0001-6101.
PUB. COUNTRY: Sweden
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197409
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19740904
ED Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19740904

L37 ANSWER 8 OF 9 MEDLINE on STN
ACCESSION NUMBER: 74262962 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4546053
TITLE: Blood transfusion requirements before and after bilateral nephrectomy in patients undergoing chronic hemodialysis.
AUTHOR: Milman N
SOURCE: Acta medica Scandinavica, (1974 Jun) 195 (6) 479-83.
Journal code: 0370330. ISSN: 0001-6101.
PUB. COUNTRY: Sweden
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197409
ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19740904
ED Entered STN: 19900310
Last Updated on STN: 19900310
Entered Medline: 19740904

L37 ANSWER 9 OF 9 MEDLINE on STN
ACCESSION NUMBER: 74148117 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4596122
TITLE: Therapeutic interactions in terminal renal failure.
AUTHOR: Moorhead J F
SOURCE: Nephron, (1974) 12 (5) 321-37.
Journal code: 0331777. ISSN: 0028-2766.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197406

Searcher : Shears 571-272-2528

ENTRY DATE: Entered STN: 19900310
Last Updated on STN: 19970203
Entered Medline: 19740619
ED Entered STN: 19900310
Last Updated on STN: 19970203
Entered Medline: 19740619

(FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO, TOXCENTER' ENTERED AT 12:16:29 ON 23 SEP 2005)
L38 2442 S "BROWNING J"?/AU
L39 1150 S "BENJAMIN C"?/AU
L40 288 S "HOCHMAN P"?/AU
L41 11 S L38 AND L39 AND L40
L42 107 S L38 AND (L39 OR L40)
L43 17 S L39 AND L40

L45 60 S (L42 OR L38 OR L39 OR L40) AND L27
L46 24 S L45 AND (DISEAS? OR DISORDER)
L47 34 S L41 OR L43 OR L46
L48 13 DUP REM L47 (21 DUPLICATES REMOVED)

L48 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:392443 CAPLUS
DOCUMENT NUMBER: 140:405481
TITLE: Anti-human **lymphotoxin B receptor (LTBR) antibodies** and fragments or lymphotoxin pathway inhibitors for treatment of immunological renal **disorders**
INVENTOR(S): Gommerman, Jennifer; **Browning, Jeffrey L.**
PATENT ASSIGNEE(S): Biogen, Inc., USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039329	A2	20040513	WO 2003-US34813	20031031
WO 2004039329	A3	20040715		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2505852	AA	20040513	CA 2003-2505852	20031031
EP 1565214	A2	20050824	EP 2003-781666	20031031
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: US 2002-422588P P 20021031

WO 2003-US34813 W 20031031

AB The disclosure relates to treatment of immunol. **disorders**, including but not limited to renal **disorders** associated with Ig deposits. The disclosure further relates to the lymphotoxin pathway. Compns. comprising lymphotoxin pathway inhibitors, especially **antibodies** or fragments specific to **LTBR** are described. The invention also disclosed inhibitory fusion protein comprising soluble **LTBR** and one or more heterologous protein domains, as well as method of evaluating efficacy of a compound for treatment of IgA nephropathy and nucleic acid hybridization method for detecting polypeptides inhibiting Ig. secretion by B cells.

L48 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2002:444385 CAPLUS
DOCUMENT NUMBER: 137:24297
TITLE: Soluble lymphotoxin-β receptors as therapeutic agents for the treatment of immunological **disease**
INVENTOR(S): **Browning, Jeffrey L.; Benjamin, Christopher D.; Hochman, Paula S.**
PATENT ASSIGNEE(S): Biogen, Inc., USA
SOURCE: U.S., 27 pp., Cont.-in-part of U.S. 5,925,351. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6403087	B1	20020611	US 1998-166	19980608
US 5925351	A	19990720	US 1995-505606	19950721
WO 9703687	A1	19970206	WO 1996-US12010	19960719
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
NZ 503818	A	20010831	NZ 1996-503818	19960719
EP 1488799	A2	20041222	EP 2004-17208	19960719
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
US 2005037003	A1	20050217	US 2002-77406	20020215

PRIORITY APPLN. INFO.:

US 1995-505606	A2	19950721
WO 1996-US12010	W	19960719
EP 1996-925393	A3	19960719
NZ 1996-313441	A1	19960719
US 1998-166	A3	19980608

AB This invention relates to compns. and methods comprising " **lymphotoxin-β receptor** blocking agents" which block **lymphotoxin-β**

receptor signaling. **Lymphotoxin**-β **receptor** blocking agents are useful for treating lymphocyte-mediated immunol. **diseases**, and more particularly, for inhibiting Th1 cell-mediated immune responses. This invention relates to soluble forms of the **lymphotoxin**-. **beta. receptor** extracellular domain that act as **lymphotoxin**-β **receptor** blocking agents. This invention also relates to the use of **antibodies** directed against either the **lymphotoxin**-β **receptor** or its ligand, surface lymphotoxin, that act as **lymphotoxin**-β **receptor** blocking agents. A novel screening method for selecting soluble receptors, **antibodies** and other agents that block **LT**-. **beta. receptor** signaling is provided.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 3 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:419176 BIOSIS
DOCUMENT NUMBER: PREV200200419176
TITLE: **Lymphotoxin-beta receptor** agonist monoclonal **antibodies** have antitumor properties.
AUTHOR(S): Lepage, Doreen J. [Reprint author]; Wilson, C. A.; Garber, E.; Bailly, V.; Ngam-Ek, A.; Ding, J.; Jarpe, M.; Lukashev, M.; Xu, X.; Szeliga, K.; Kelly, R.; Fawell, S.; Tao, N.; Boral, A.; Myers, J.; **Browning, J.**
CORPORATE SOURCE: Biogen, Inc., Cambridge, MA, USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2002) Vol. 43, pp. 1005. print.
Meeting Info.: 93rd Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA. April 06-10, 2002.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Aug 2002
Last Updated on STN: 7 Aug 2002

L48 ANSWER 4 OF 13 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2000-317848 [27] WPIDS
DOC. NO. CPI: C2000-096214
TITLE: Lymphotoxin-beta receptor blocking agent used to induce an antiviral response to treat e.g. Ebola virus, viral-induced systemic shock and respiratory distress.
DERWENT CLASS: B04 D16
INVENTOR(S): AHMED, R; **BROWNING, J**; PUGLIELLI, M; **BROWNING, J L**
PATENT ASSIGNEE(S): (BIOJ) BIOGEN INC; (UYEM-N) UNIV EMORY; (AHME-I) AHMED R; (BROW-I) BROWNING J; (PUGL-I) PUGLIELLI M; (BROW-I) BROWNING J L
COUNTRY COUNT: 86
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000021558	A1	20000420	(200027)*	EN	40
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZW					
AU 9962964	A	20000501	(200036)		
NO 2001001757	A	20010608	(200141)		
EP 1119370	A1	20010801	(200144)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
BR 9915025	A	20010814	(200154)		
CZ 2001001272	A3	20010912	(200158)		
SK 2001000466	A3	20011106	(200176)		
US 2002001585	A1	20020103	(200207)		
KR 2001080073	A	20010822	(200213)		
CN 1323223	A	20011121	(200218)		
HU 2001003773	A2	20020128	(200222)		
JP 2002527403	W	20020827	(200271)		50
NZ 510560	A	20030926	(200366)		
US 2004198635	A1	20041007	(200466)		
AU 777492	B2	20041021	(200501)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2000021558	A1		WO 1999-US23477	19991008
AU 9962964	A		AU 1999-62964	19991008
NO 2001001757	A		WO 1999-US23477	19991008
			NO 2001-1757	20010406
EP 1119370	A1		EP 1999-950270	19991008
			WO 1999-US23477	19991008
BR 9915025	A		BR 1999-15025	19991008
			WO 1999-US23477	19991008
CZ 2001001272	A3		WO 1999-US23477	19991008
			CZ 2001-1272	19991008
SK 2001000466	A3		WO 1999-US23477	19991008
			SK 2001-466	19991008
US 2002001585	A1	Provisional	US 1998-103662P	19981009
		Cont of	WO 1999-US23477	19991008
			US 2001-829031	20010409
KR 2001080073	A		KR 2001-704493	20010409
CN 1323223	A		CN 1999-811955	19991008
HU 2001003773	A2		WO 1999-US23477	19991008
			HU 2001-3773	19991008
JP 2002527403	W		WO 1999-US23477	19991008
			JP 2000-575531	19991008
NZ 510560	A		NZ 1999-510560	19991008
			WO 1999-US23477	19991008
US 2004198635	A1	Provisional	US 1998-103662P	19981009
		Cont of	WO 1999-US23477	19991008
		Cont of	US 2001-829031	20010409
			US 2004-829720	20040421
AU 777492	B2		AU 1999-62964	19991008

Searcher : Shears 571-272-2528

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9962964	A	Based on	WO 2000021558
EP 1119370	A1	Based on	WO 2000021558
BR 9915025	A	Based on	WO 2000021558
CZ 2001001272	A3	Based on	WO 2000021558
SK 2001000466	A3	Based on	WO 2000021558
HU 2001003773	A2	Based on	WO 2000021558
JP 2002527403	W	Based on	WO 2000021558
NZ 510560	A	Based on	WO 2000021558
AU 777492	B2	Previous Publ.	AU 9962964
		Based on	WO 2000021558

PRIORITY APPLN. INFO: US 1998-103662P 19981009; US
2001-829031 20010409; US
2004-829720 20040421

AN 2000-317848 [27] WPIDS

AB WO 200021558 A UPAB: 20000606

NOVELTY - Inducing an antiviral response through administration of an agent which blocks the binding of lymphotoxin- beta (LT-B), a tumor necrosis factor (TNF), to its receptor, is new.

ACTIVITY - Antiviral.

Treating lymphocytic choriomeningitis virus (LCMV)-13 infected NZB mice with an LTB blocking agent e.g. LTB-R-Ig fusion protein, increased their survival rate by 73%.

MECHANISM OF ACTION - Inhibitor of the lymphotoxin- beta -receptor and/or herpes virus entry mediator (HVEM) signaling pathway.

USE - The agents are used to induce an antiviral response in an individual infected with Sin Nombre Virus, Ebola virus, Marburg virus, Lassa virus or Dengue (claimed). The agents used can treat viral-induced systemic shock and respiratory distress in an individual. The individuals treated are vertebrates, particularly domestic animals, sports animals and primates, including humans.

ADVANTAGE - Currently no vaccine is available for treating Sin Nombre, Ebola, Marburg, Lassa and Dengue viruses and the only treatment is preventative through education on **disease** transmission.

Dwg.0/5

L48 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2000:107474 CAPLUS
DOCUMENT NUMBER: 132:263919
TITLE: Systematic mutational mapping of sites on human interferon-β-1a that are important for receptor binding and functional activity
AUTHOR(S): Runkel, Laura; DeDios, Carole; Karpusas, Michael; Betzenhauser, Matthew; Muldowney, Celine; Zafari, Mohammad; **Benjamin, Christopher D.**; Miller, Stephan; **Hochman, Paula S.**; Whitty, Adrian
CORPORATE SOURCE: Biogen Inc., Cambridge, MA, 02142, USA
SOURCE: Biochemistry (2000), 39(10), 2538-2551
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A systematic mutational anal. of human interferon-β-1a (IFN-β) was performed to identify regions on the surface of the mol. that are important for receptor binding and for functional activity. The crystal structure of IFN-β-1a was used to design a panel of 15 mutant proteins, in each of which a contiguous group of 2-8 surface residues was mutated, in most instances to alanine. The mutants were analyzed for activity in vitro in antiviral and in anti-proliferation assays, and for their ability to bind to the type I IFN (ifnar1/ifnar2) receptor on Daudi cells and to a soluble ifnar2 fusion protein (ifnar2-Fc). Abolition of binding to ifnar2-Fc for mutants A2, AB1, AB2, and E established that the ifnar2 binding site on IFN-β comprises parts of the A helix, the AB loop, and the E helix. Mutations in these areas, which together define a contiguous patch of the IFN-β surface, also resulted in reduced affinity for binding to the receptor on cells and in redns. in activity of 5-50-fold in functional assays. A second receptor interaction site, concluded to be the ifnar1 binding site, was identified on the opposite face of the mol. Mutations in this region, which encompasses parts of the B, C, and D helixes and the DE loop, resulted in disparate effects on receptor binding and on functional activity. Anal. of anti-proliferation activity as a function of the level of receptor occupancy allowed mutational effects on receptor activation to be distinguished from effects on receptor binding. The results suggest that the binding energy from interaction of IFN-β with ifnar2 serves mainly to stabilize the bound IFN/receptor complex, whereas the binding energy generated by interaction of certain regions of IFN-β with ifnar1 is not fully expressed in the observed affinity of binding but instead serves to selectively stabilize activated states of the receptor.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 6 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1999:435938 BIOSIS
DOCUMENT NUMBER: PREV199900435938
TITLE: Soluble **lymphotoxin-beta receptors** and anti-lymphotoxin receptor and ligand **antibodies** as therapeutic agents for the treatment of immunological **disease**.
AUTHOR(S): **Browning, Jeffrey L.** [Inventor, Reprint author]; **Benjamin, Christopher D.** [Inventor]; **Hochman, Paula S.** [Inventor]
CORPORATE SOURCE: Slone Epidemiology Unit, School of Public Health, Boston University School of Medicine, Brookline, MA, USA
ASSIGNEE: Biogen, Inc.
PATENT INFORMATION: US 5925351 19990720
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Jul. 20, 1999) Vol. 1224, No. 3. print.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Oct 1999
Last Updated on STN: 18 Oct 1999

L48 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 1998:268386 CAPLUS
DOCUMENT NUMBER: 129:3859
TITLE: Soluble **lymphotoxin-beta receptors**, anti-lymphotoxin receptor **antibodies**, and anti-lymphotoxin ligand **antibodies** as therapeutic agents for the treatment of immunological **diseases**
INVENTOR(S): **Browning, Jeffrey; Hochman, Paula Susan**; Rennert, Paul D.; Mackay, Fabienne
PATENT ASSIGNEE(S): Biogen, Inc., USA; Browning, Jeffrey; Hochman, Paula Susan; Rennert, Paul D.; Mackay, Fabienne
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9817313	A2	19980430	WO 1997-US19436		19971024
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2269614	AA	19980430	CA 1997-2269614		19971024
AU 9850896	A1	19980515	AU 1998-50896		19971024
AU 726357	B2	20001102			
BR 9712670	A	19991019	BR 1997-12670		19971024
EP 954333	A2	19991110	EP 1997-913798		19971024
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
CN 1237910	A	19991208	CN 1997-199906		19971024
NZ 335353	A	20000929	NZ 1997-335353		19971024
JP 2001502697	T2	20010227	JP 1998-519688		19971024
NO 9901926	A	19990625	NO 1999-1926		19990422
KR 2000052800	A	20000825	KR 1999-703619		19990424
BG 63565	B1	20020531	BG 1999-103416		19990520
US 2002197254	A1	20021226	US 2001-3211		20011031
PRIORITY APPLN. INFO.:			US 1996-29060P	P	19961025
			WO 1997-US19436	W	19971024
			US 1999-299139	A1	19990423

AB Compns. and methods comprising "**lymphotoxin-β receptor** blocking agents" which block **lymphotoxin-. beta. receptor** signalling and are useful for altering immunol. **diseases**, and particularly **antibody** mediated immune responses. The **lymphotoxin -β receptor** blocking agents are monoclonal **antibodies**, soluble **lymphotoxin-β receptor**, anti-lymphotoxin ligand **antibodies**, or fusion protein of soluble **lymphotoxin-β**

receptor and **Ig Fc** domain. The immunol. **disease** is e.g. AIDS, HIV infection, graft rejection, etc. Antiviral agent, anti-AIDS agent, or anti-CD40L and other carrier or adjuvant are also included in the remedy.

L48 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 1998:801597 CAPLUS
DOCUMENT NUMBER: 130:208275
TITLE: Both the lymphotoxin and tumor necrosis factor pathways are involved in experimental murine models of colitis
AUTHOR(S): MacKay, Fabienne; **Browning, Jeffrey L.**; Lawton, Pornsri; Shah, Samir A.; Comiskey, Martina; Bhan, Atul K.; Mizoguchi, Emiko; Terhorst, Cox; Simpson, Stephen J.
CORPORATE SOURCE: Department of Immunology, Inflammation and Cell Biology, Biogen, Cambridge, USA
SOURCE: Gastroenterology (1998), 115(6), 1464-1475
CODEN: GASTAB; ISSN: 0016-5085
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Membrane lymphotoxin (LT) α/β, a member of the tumor necrosis factor (TNF) family of immune regulatory mols., is involved both in the development of secondary lymphoid tissues and the maintenance of organized lymphoid tissues in the adult. Defects observed in the mucosal immune system in animals with a genetically disrupted LTα/β pathway coupled with the expression of LTα/β in activated T cells motivated an examination of the importance of this pathway in exptl. colitis. Soluble **LT. beta. receptor** (**LTβ R**) Ig fusion protein was used to inhibit the LTα/β axis in two independent rodent models of colitis: CD45RBhi CD4+-reconstituted SCID mice and bone marrow-transplanted tgε26 mice (BM → tgε26). Treatment with **LT.beta.R** Ig attenuated the development of both the clin. and histol. manifestations of the **disease** in these two murine models of colitis. Given the success of TNF inhibitors in the treatment of human Crohn's **disease**, the effects of **LT.beta.R** Ig have been compared with **antibody** to TNF in the BM → tgε26 model, and both treatments were equally efficacious. The LT pathway plays a role in the development of colitis as important as that of the TNF system and, therefore, represents a potential novel intervention point for the treatment of inflammatory bowel **disease**.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 1997:205227 CAPLUS
DOCUMENT NUMBER: 126:198559
TITLE: Soluble **lymphotoxin-β receptors** and anti-lymphotoxin receptor and ligand **antibodies**, as therapeutic agents for the treatment of immunological **disease**
INVENTOR(S): **Browning, Jeffrey L.**; **Benjamin,**

Christopher D.; Hochman, Paula S.
PATENT ASSIGNEE(S): Biogen, Inc., USA; Browning, Jeffrey L.; Benjamin, Christopher D.; Hochman, Paula S.
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9703687	A1	19970206	WO 1996-US12010	19960719
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
US 5925351	A	19990720	US 1995-505606	19950721
CA 2227477	AA	19970206	CA 1996-2227477	19960719
AU 9665912	A1	19970218	AU 1996-65912	19960719
AU 715407	B2	20000203		
EP 840616	A1	19980513	EP 1996-925393	19960719
EP 840616	B1	20041013		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
CN 1195294	A	19981007	CN 1996-196770	19960719
BR 9609716	A	19990706	BR 1996-9716	19960719
JP 11510488	T2	19990914	JP 1996-506919	19960719
NZ 313441	A	20000728	NZ 1996-313441	19960719
NZ 503818	A	20010831	NZ 1996-503818	19960719
PL 186911	B1	20040331	PL 1996-324622	19960719
AT 279205	E	20041015	AT 1996-925393	19960719
EP 1488799	A2	20041222	EP 2004-17208	19960719
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
PT 840616	T	20041231	PT 1996-925393	19960719
EE 4419	B1	20050215	EE 1998-13	19960719
ES 2225889	T3	20050316	ES 1996-925393	19960719
NO 9800172	A	19980323	NO 1998-172	19980114
FI 9800122	A	19980319	FI 1998-122	19980120
BG 63330	B1	20011031	BG 1998-102265	19980220
US 6403087	B1	20020611	US 1998-166	19980608
HK 1010832	A1	20050527	HK 1998-111990	19981113
US 6669941	B1	20031230	US 1999-303262	19990430
AU 748656	B2	20020606	AU 2000-27793	20000414
US 2005037003	A1	20050217	US 2002-77406	20020215

PRIORITY APPLN. INFO.:	US 1995-505606	A	19950721
	EP 1996-925393	A3	19960719
	NZ 1996-313441	A1	19960719
	WO 1996-US12010	W	19960719
	US 1998-166	A3	19980608

AB This invention relates to compns. and methods comprising "

lymphotoxin-β receptor blocking agents", which block **lymphotoxin-β receptor** signalling. **Lymphotoxin-β receptor** blocking agents are useful for treating lymphocyte-mediated immunol. **diseases**, and more particularly, for inhibiting Th1 cell-mediated immune responses, e.g. delayed type hypersensitivity, contact hypersensitivity, tuberculin-type hypersensitivity, granulomatous, organ transplant rejection, and others. This invention also relates to the use of **antibodies** directed against either the **lymphotoxin-**. **beta. receptor** or its ligand, surface lymphotoxin, that act as **lymphotoxin-β receptor** blocking agents. A novel screening method for selecting soluble receptors, **antibodies** and other agents that block **LT -β receptor** signalling is provided.

L48 ANSWER 10 OF 13 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:138412 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA12615198559A
TITLE: Soluble **lymphotoxin-β receptors** and anti-lymphotoxin receptor and ligand **antibodies**, as therapeutic agents for the treatment of immunological **disease**
AUTHOR(S): **Browning, Jeffrey L.; Benjamin, Christopher D.; Hochman, Paula S.**
CORPORATE SOURCE: ASSIGNEE: Hochman, Paula S.
PATENT INFORMATION: WO 973687 A1 6 Feb 1997
SOURCE: (1997) PCT Int. Appl., 75 pp.
CODEN: PIXXD2.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 1997:205227
LANGUAGE: English
ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020626

AB This invention relates to compns. and methods comprising " **lymphotoxin-β receptor** blocking agents", which block **lymphotoxin-β receptor** signalling. **Lymphotoxin-β receptor** blocking agents are useful for treating lymphocyte-mediated immunol. **diseases**, and more particularly, for inhibiting Th1 cell-mediated immune responses, e.g. delayed type hypersensitivity, contact hypersensitivity, tuberculin-type hypersensitivity, granulomatous, organ transplant rejection, and others. This invention also relates to the use of **antibodies** directed against either the **lymphotoxin-**. **beta. receptor** or its ligand, surface lymphotoxin, that act as **lymphotoxin-β receptor** blocking agents. A novel screening method for selecting soluble receptors, **antibodies** and other agents that block **LT -β receptor** signalling is provided.

L48 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 1997:637126 CAPLUS
DOCUMENT NUMBER: 127:317911
TITLE: Characterization of lymphotoxin-αβ complexes on the surface of mouse lymphocytes

AUTHOR(S): **Browning, Jeffrey L.**; Sizing, Irene Dougas; Lawton, Pornsri; Bourdon, Paul R.; Rennert, Paul D.; Majeau, Gerard R.; Ambrose, Christine M.; Hession, Catherine; Miatkowski, Konrad; Griffiths, David A.; Ngam-ek, Apinya; Christopher, Werner Meier; **Benjamin, Christopher D.**; **Hochman, Paula s.**

CORPORATE SOURCE: Dep. Immunol. Inflammation Cell Biol, Protein Eng., Molecular Genetics, Biogen, Cambridge, MA, 02142, USA

SOURCE: Journal of Immunology (1997), 159(7), 3288-3298
CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The lymphotoxin-αβ complex (LTαβ) is found on the surface of activated lymphocytes and binds to a specific receptor called the LTβ receptor (LTβR). In the mouse, signaling through this pathway is important for lymph node development and splenic organization, yet the biochem. properties of murine LTα and LTβ are essentially unknown. Here the authors used soluble receptor-Ig forms of LTβR and TNF-R55 and mAbs specific for murine LTα, LTβ, and LTβR to characterize the appearance of surface LTαβ complexes and LTβR on several common murine cell lines. Cells that bound LTβR also bound anti-LTα and anti-LTβmAbs in a FACS anal. The ability of these reagents to discriminate between surface TNF and LT was verified by anal. of surface TNF-pos., LPS-activated murine RAW 264.7 monocytes. Primary mouse leukocytes from spleen, thymus, lymph node, and peritoneum were activated in vitro, and CD4+ and CD8+ T cells as well as B cells expressed surface LT ligand but not the LTβR. Conversely, elicited peritoneal monocytes/macrophages were surface LT neg. yet LTβR pos. Thus, on mononuclear cells, surface LT complexes and receptor are expressed similarly in mice and man, and the tools described herein form the foundation for study of the functional roles of the LT system in the mouse.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 8

ACCESSION NUMBER: 1997:482951 CAPLUS

DOCUMENT NUMBER: 127:219374

TITLE: Antibodies to lymphotoxin α (LTα) and LTβ recognize different glial cell types in the central nervous system

AUTHOR(S): Cannella, Barbara; Dougas Sizing, Irene; **Benjamin, Christopher D.**; **Browning, Jeffrey L.**; Raine, Cedric S.

CORPORATE SOURCE: Department of Pathology, Rose F. Kennedy Center for Research in Mental Retardation and Human Development, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY, 10461, USA

SOURCE: Journal of Neuroimmunology (1997), 78(1-2), 172-179
CODEN: JNRIDW; ISSN: 0165-5728

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The cytokine lymphotoxin (LT) is known to exist in two forms, secreted LTα and a membrane-bound LTα/β complex. LTα shares the same receptor as tumor necrosis factor α and LTβ is recognized by its receptor, **LT.beta.R**. Since LT has been associated with oligodendrocyte pathol., the present study has examined the expression of these mols. by immunocytochem. in **diseased** and normal CNS tissue, with a panel of monoclonal **antibodies** (mAb) to LTα, LTβ and **LT.beta.R**. Of three mAb to LTβ, two (B27 and C37) gave specific membrane staining on astrocytes, as well as lymphocytes. The third anti-LTβ mAb, B9, was selectively immunoreactive for oligodendrocytes, suggesting specific recognition sites. The reactivity was not specific for multiple sclerosis (MS) since oligodendrocytes in normal and non-MS CNS tissue also displayed positivity. MAb to **LT.beta.R** reacted with astrocytes only, giving a punctate membrane staining pattern suggestive of receptor sites. MAb to LTα gave strong reactivity on lymphocytes in active MS lesions and weak reactivity on microglia within lesion areas. These results show that mAb to LTα and LTβ recognize different cell types within the CNS. Furthermore, individual mAb against LTβ were capable of distinguishing between astrocytes and oligodendrocytes, perhaps indicative of different epitopes on LTβ. The presence of **LTβ R** on astrocytes suggests possible interactions between infiltrating lymphocytes and astrocytes via the LT pathway.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 13 OF 13 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1995:385179 BIOSIS
DOCUMENT NUMBER: PREV199598399479
TITLE: Signalling through the lymphotoxin-beta receptor in conjunction with interferon-gamma induces the death of a human tumor line.
AUTHOR(S): **Browning, Jeffrey L.**; Miatkowski, Konrad; Griffiths, David; Dougas, Irene; Majeau, Gerald; **Benjamin, Chris; Hochman, Paula**; Meier, Werner
CORPORATE SOURCE: Biogen, Cambridge, MA, USA
SOURCE: 9TH INTERNATIONAL CONGRESS OF IMMUNOLOGY. (1995) pp. 772. The 9th International Congress of Immunology. Publisher: 9th International Congress of Immunology, San Francisco, California, USA. Meeting Info.: Meeting Sponsored by the American Association of Immunologists and the International Union of Immunological Societies. San Francisco, California, USA. July 23-29, 1995.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 1 Sep 1995
Last Updated on STN: 1 Sep 1995

FILE 'HOME' ENTERED AT 12:19:51 ON 23 SEP 2005

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     (FILE 'CAPLUS' ENTERED AT 12:03:04 ON 23 SEP 2005)
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L*** DEL     36 S L27 AND (TREAT? OR THERAP? OR PREVENT?)
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                D TI AU 1-4
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                D KWIC
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L26         279 SEA ABB=ON  PLU=ON  L25 OR (LYMPHOTOXIN OR LYMPHO TOXIN OR .
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     JICST-EPLUS, JAPIO, TOXCENTER' ENTERED AT 12:10:54 ON 23 SEP 2005
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L31          44 DUP REM L30 (45 DUPLICATES REMOVED)
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L33        2150 SEA ABB=ON  PLU=ON  LYMPHOTOXIN/CT
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                E "IMMUNOGLOBULINS, FC"/CT 5
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L35       63785 SEA ABB=ON  PLU=ON  ANTIBODIES/CT
L36         118 SEA ABB=ON  PLU=ON  L33 AND (L34 OR L35)
L37           9 SEA ABB=ON  PLU=ON  L36 AND (THERAPY OR THERAPEUTIC
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                D QUE
                D 1-9 .BEVERLYMED

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     JICST-EPLUS, JAPIO, TOXCENTER' ENTERED AT 12:16:29 ON 23 SEP 2005
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L40         288 SEA ABB=ON  PLU=ON  "HOCHMAN P"?/AU
L41          11 SEA ABB=ON  PLU=ON  L38 AND L39 AND L40
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Searcher : Shears 571-272-2528

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L44          225 SEA ABB=ON  PLU=ON  (L42 OR L38 OR L39 OR L40) AND L26
L45           60 SEA ABB=ON  PLU=ON  (L42 OR L38 OR L39 OR L40) AND L27
L*** DEL      70 S L41 OR L43 OR L45
L*** DEL      25 DUP REM L46 (45 DUPLICATES REMOVED)
L46           24 SEA ABB=ON  PLU=ON  L45 AND (DISEAS? OR DISORDER)
L47           34 SEA ABB=ON  PLU=ON  L41 OR L43 OR L46
L48           13 DUP REM L47 (21 DUPLICATES REMOVED)
                 D 1-13 IBIB ABS

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     FILE CAPLUS

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     FILE LAST UPDATED: 22 Sep 2005  (20050922/ED)

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     DICTIONARY FILE UPDATES:  22 SEP 2005  HIGHEST RN 863708-11-6

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     * The CA roles and document type information have been removed from *
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     * effective March 20, 2005.  A new display format, IDERL, is now    *
     * available and contains the CA role and document type information. *
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     for details.

                    Searcher    :     Shears     571-272-2528
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FILE MEDLINE
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On December 19, 2004, the 2005 MeSH terms were loaded.

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http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 21 September 2005 (20050921/ED)

FILE RELOADED: 19 October 2003.

FILE EMBASE
FILE COVERS 1974 TO 22 Sep 2005 (20050922/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE WPIDS
FILE LAST UPDATED: 20 SEP 2005 <20050920/UP>
MOST RECENT DERWENT UPDATE: 200560 <200560/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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Searcher : Shears 571-272-2528

>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT
DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX
FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS: http://www.thomsonderwent.com/dwpifv <<<

>>> THE CPI AND EPI MANUAL CODES HAVE BEEN REVISED FROM UPDATE 200501.
PLEASE CHECK:
http://thomsonderwent.com/support/dwpiref/reftools/classification/code
FOR DETAILS. <<<

FILE CONFSCI
FILE COVERS 1973 TO 25 May 2005 (20050525/ED)

FILE SCISEARCH

FILE COVERS 1974 TO 22 Sep 2005 (20050922/ED)

SCISEARCH has been reloaded, see HELP RLOAD for details.

FILE JICST-EPLUS
FILE COVERS 1985 TO 19 SEP 2005 (20050919/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED
TERM (/CT) THESAURUS RELOAD.

FILE JAPIO
FILE LAST UPDATED: 5 SEP 2005 <20050905/UP>
FILE COVERS APR 1973 TO APRIL 28, 2005

<<< GRAPHIC IMAGES AVAILABLE >>>

FILE TOXCENTER

FILE COVERS 1907 TO 20 Sep 2005 (20050920/ED)

This file contains CAS Registry Numbers for easy and accurate substanc
identification.

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See HELP CONTENT for more information.

TOXCENTER thesauri in the /CN, /CT, and /MN fields incorporate the
MeSH 2005 vocabulary. See http://www.nlm.nih.gov/mesh/ and
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html for a
description of changes.

```
=> d his l25- ful

     (FILE 'REGISTRY' ENTERED AT 11:54:40 ON 23 SEP 2005)
                D SCAN

     FILE 'HOME' ENTERED AT 11:59:22 ON 23 SEP 2005
                D COST
                D COST
                D COST

     FILE 'REGISTRY' ENTERED AT 12:01:39 ON 23 SEP 2005
                E LYMPHOTOXIN BETA RECEPTOR/CN 5
L*** DEL        0 S LYPHOTOXIN BETA RECEPTOR?/CN
L25             1 SEA ABB=ON  PLU=ON  LYMPHOTOXIN BETA RECEPTOR?/CN

     FILE 'CAPLUS' ENTERED AT 12:03:04 ON 23 SEP 2005
L*** DEL      231 S L25 OR (LYMPHOTOXIN OR LYMPHO TOXIN OR LT)(W)(BR OR BETA(
L*** DEL       60 S L26 AND ANTIBOD?
L*** DEL       36 S L27 AND (TREAT? OR THERAP? OR PREVENT?)
L*** DEL        4 S L28 AND HOCHMAN ?/AU
                  D TI AU 1-4
L*** DEL        4 S L29 AND (IG OR IMMUNOGLOBULIN OR IMMUNO GLOBULIN)
                  D KWIC
L*** DEL       48 S L26(L)(ANTIBOD? OR FC(1A)(IMMUNOGLOBULIN OR IG OR IMMUNO
L*** DEL       23 S L27(L)(TREAT? OR THERAP? OR PREVENT?)
L*** DEL        3 S L28 AND HOCHMAN ?/AU
                  D TI AU 1-3
                  D KWIC 3
L26           279 SEA ABB=ON  PLU=ON  L25 OR (LYMPHOTOXIN OR LYMPHO TOXIN OR
                  LT)(W)(BR OR (B OR BETA)(1W)(RECEPTOR OR R)) OR LTBR
L27            58 SEA ABB=ON  PLU=ON  L26(L)(ANTIBOD? OR FC(1A)(IMMUNOGLOBULI
                  N OR IG OR IMMUNO GLOBULIN))
L28            27 SEA ABB=ON  PLU=ON  L27(L)(TREAT? OR THERAP? OR PREVENT?)
L*** DEL        0 S L28 NOT (PY=>1995 OR PD=>19940721)
L29             0 SEA ABB=ON  PLU=ON  L28 NOT (PY=>1995 OR PD=>19950721)

     FILE 'REGISTRY' ENTERED AT 12:10:49 ON 23 SEP 2005

     FILE 'CAPLUS' ENTERED AT 12:10:49 ON 23 SEP 2005
                D QUE L29
                D L28 1-27 .BEVSTR

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     JICST-EPLUS, JAPIO, TOXCENTER' ENTERED AT 12:10:54 ON 23 SEP 2005
L30            89 SEA ABB=ON  PLU=ON  L28
L31            44 DUP REM L30 (45 DUPLICATES REMOVED)
                  D 1-44 IBIB ABS

     FILE 'MEDLINE' ENTERED AT 12:12:31 ON 23 SEP 2005
                E LYMPHOTOXIN BETA RECEPTOR/CT 5
L32             0 SEA ABB=ON  PLU=ON  "LYMPHOTOXIN BETA RECEPTOR"/CT
                  E LYMPHOTOXINS/CT 5
                  E LYMPHOTOXIN/CT 5
L33          2150 SEA ABB=ON  PLU=ON  LYMPHOTOXIN/CT
                  E IMMUNOGLOBULIN FC/CT 5
                  E FC IMMUNOGLOBULINS/CT 5
                  E "IMMUNOGLOBULINS, FC"/CT 5
L34          3655 SEA ABB=ON  PLU=ON  "IMMUNOGLOBULINS, FC"/CT
                  E ANTIBODIES/CT 5
```

```
L35        63785 SEA ABB=ON  PLU=ON  ANTIBODIES/CT
L36          118 SEA ABB=ON  PLU=ON  L33 AND (L34 OR L35)
L37            9 SEA ABB=ON  PLU=ON  L36 AND (THERAPY OR THERAPEUTIC
                 USE)/CT
                 D QUE
                 D 1-9 .BEVERLYMED

     FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     JICST-EPLUS, JAPIO, TOXCENTER' ENTERED AT 12:16:29 ON 23 SEP 2005
L38         2442 SEA ABB=ON  PLU=ON  "BROWNING J"?/AU
L39         1150 SEA ABB=ON  PLU=ON  "BENJAMIN C"?/AU
L40          288 SEA ABB=ON  PLU=ON  "HOCHMAN P"?/AU
L41           11 SEA ABB=ON  PLU=ON  L38 AND L39 AND L40
L42          107 SEA ABB=ON  PLU=ON  L38 AND (L39 OR L40)
L43           17 SEA ABB=ON  PLU=ON  L39 AND L40
L44          225 SEA ABB=ON  PLU=ON  (L42 OR L38 OR L39 OR L40) AND L26
L45           60 SEA ABB=ON  PLU=ON  (L42 OR L38 OR L39 OR L40) AND L27
L*** DEL      70 S L41 OR L43 OR L45
L*** DEL      25 DUP REM L46 (45 DUPLICATES REMOVED)
L46           24 SEA ABB=ON  PLU=ON  L45 AND (DISEAS? OR DISORDER)
L47           34 SEA ABB=ON  PLU=ON  L41 OR L43 OR L46
L48           13 DUP REM L47 (21 DUPLICATES REMOVED)
                 D 1-13 IBIB ABS

     FILE 'HOME' ENTERED AT 12:19:51 ON 23 SEP 2005


     FILE CAPLUS

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     FILE COVERS 1907 - 23 Sep 2005  VOL 143 ISS 14
     FILE LAST UPDATED: 22 Sep 2005  (20050922/ED)

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

       This file contains CAS Registry Numbers for easy and accurate
       substance identification.

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   22 SEP 2005  HIGHEST RN 863708-11-6
     DICTIONARY FILE UPDATES:  22 SEP 2005  HIGHEST RN 863708-11-6

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

       Please note that search-term pricing does apply when
```

conducting SmartSELECT searches.

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**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from  *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************
```

Structure search iteration limits have been increased. See HELP SLIMI for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

FILE HOME

FILE MEDLINE
FILE LAST UPDATED: 22 SEP 2005 (20050922/UP). FILE COVERS 1950 TO DA

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 21 September 2005 (20050921/ED)

FILE RELOADED: 19 October 2003.

FILE EMBASE
FILE COVERS 1974 TO 22 Sep 2005 (20050922/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE WPIDS
FILE LAST UPDATED: 20 SEP 2005 <20050920/UP>

Searcher : Shears 571-272-2528

MOST RECENT DERWENT UPDATE: 200560 <200560/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE http://thomsonderwent.com/coverage/latestupdates/ <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER GUIDES, PLEASE VISIT:
http://thomsonderwent.com/support/userguides/ <<<

>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS: http://www.thomsonderwent.com/dwpifv <<<

>>> THE CPI AND EPI MANUAL CODES HAVE BEEN REVISED FROM UPDATE 200501. PLEASE CHECK:
http://thomsonderwent.com/support/dwpiref/reftools/classification/code FOR DETAILS. <<<

FILE CONFSCI
FILE COVERS 1973 TO 25 May 2005 (20050525/ED)

FILE SCISEARCH

FILE COVERS 1974 TO 22 Sep 2005 (20050922/ED)

SCISEARCH has been reloaded, see HELP RLOAD for details.

FILE JICST-EPLUS
FILE COVERS 1985 TO 19 SEP 2005 (20050919/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE JAPIO
FILE LAST UPDATED: 5 SEP 2005 <20050905/UP>
FILE COVERS APR 1973 TO APRIL 28, 2005

<<< GRAPHIC IMAGES AVAILABLE >>>

FILE TOXCENTER

FILE COVERS 1907 TO 20 Sep 2005 (20050920/ED)

This file contains CAS Registry Numbers for easy and accurate substanc identification.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TOXCENTER has been enhanced with new files segments and search fields. See HELP CONTENT for more information.

TOXCENTER thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary. See http://www.nlm.nih.gov/mesh/ and

http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html for a description of changes.

Searcher : Shears 571-272-2528

arthritis, psoriasis, Crohn's disease, infections, malignancies or neurodegenerative diseases.
Dwg.0/4

L31 ANSWER 8 OF 44 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-201265 [19] WPIDS
CROSS REFERENCE: 1997-480153 [44]; 1999-430394 [36]; 1999-590729 [50]; 2000-594264 [56]; 2002-556723 [59]; 2002-626537 [67]; 2003-810570 [76]
DOC. NO. CPI: C2004-079546
TITLE: Isolated apoptosis inducing molecule II polypeptide, useful for treating, preventing, ameliorating, diagnosing or prognosing autoimmune diseases such as multiple sclerosis, rheumatoid arthritis, aplastic anemia.
DERWENT CLASS: A96 B04 B05 D16 D22
INVENTOR(S): EBNER, R; RUBEN, S M; ULLRICH, S; YU, G; ZHAI, Y
PATENT ASSIGNEE(S): (HUMA-N) HUMAN GENOME SCI INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2004009147	A1	20040115	(200419)*		189

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2004009147	A1	Provisional	US 1996-13923P	19960322
		Provisional	US 1996-30157P	19961031
		CIP of	US 1997-822953	19970321
		CIP of	US 1998-3886	19980107
		CIP of	US 1998-27287	19980220
		Provisional	US 1998-75409P	19980220
		CIP of	US 1999-252656	19990219
		Provisional	US 1999-124041P	19990311
		Provisional	US 1999-137457P	19990604
		Provisional	US 1999-142657P	19990706
		Provisional	US 1999-148326P	19990811
		Provisional	US 1999-168380P	19991202
		CIP of	US 2000-523323	20000310
		Provisional	US 2002-360234P	20020301
			US 2003-375680	20030228

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 2004009147	A1	CIP of	US 6479254
		CIP of	US 6495520
		CIP of	US 6635743

PRIORITY APPLN. INFO: US 2003-375680 20030228; US 1996-13923P 19960322; US 1996-30157P 19961031; US 1997-822953 19970321; US 1998-3886 19980107; US 1998-27287 19980220; US

Searcher : Shears 571-272-2528

1998-75409P	19980220; US
1999-252656	19990219; US
1999-124041P	19990311; US
1999-137457P	19990604; US
1999-142657P	19990706; US
1999-148326P	19990811; US
1999-168380P	19991202; US
2000-523323	20000310; US
2002-360234P	20020301

AN 2004-201265 [19] WPIDS

CR 1997-480153 [44]; 1999-430394 [36]; 1999-590729 [50]; 2000-594264 [56]; 2002-556723 [59]; 2002-626537 [67]; 2003-810570 [76]

AB US2004009147 A UPAB: 20040318

NOVELTY - An isolated apoptosis inducing molecule II (AIM II) polypeptide (I) comprising amino acid residues 83-240 of a fully defined sequence (S1) of 240 amino acids as given in specification, and at least 90% or 95% identical to amino acid residues 83-240 or 60-240 of (S1), is new.

DETAILED DESCRIPTION - An isolated apoptosis inducing molecule II (AIM II) polypeptide (I) comprising amino acid residues 83-240 of a fully defined sequence (S1) of 240 amino acids as given in specification, and at least 90% or 95% identical to amino acid residues 83-240 or 60-240 of (S1), where the polypeptide is covalently attached to polyethylene glycol having an average molecule weight chosen from 2000-10000, 15000 and 20000, is new.

INDEPENDENT CLAIMS are also included for the following:

(1) **treating** (M1) graft versus host disease, immunodeficiency, or autoimmunity, involves administering to an individual a first **therapeutic** agent comprising an **antibody** which binds to a polypeptide consisting of amino acid residues 1-240 of (S1) and a second **therapeutic** agent chosen from a tumor necrosis factor, an immunosuppressive agent, an antibiotic, an anti-inflammatory agent, chemotherapeutic agent, cytokine, an angiogenic agent, and fibroblast growth factor;

(2) a composition (II) comprising a first **therapeutic** agent comprising an **antibody** which binds to a polypeptide consisting of amino acids 1-240 of (S1), and a second **therapeutic** agent chosen from a tumor necrosis factor, an immunosuppressive agent, an antibiotic, an anti-inflammatory agent, a chemotherapeutic agent, a cytokine, an angiogenic agent, and a fibroblast growth factor;

(3) **treating** (M2) immunodeficiency or cancer, involves administering to an individual a first **therapeutic** agent comprising an isolated polypeptide comprising amino acid residues at least 90% identical to amino acid residues 83-240 of (S1), and a second **therapeutic** agent (STA) chosen from an antibiotic, an anti-inflammatory agent, an angiogenic agent, and a fibroblast growth factor;

(4) **treating** immunodeficiency or cancer, involves administering to an individual amounts of a first **therapeutic** agent comprising an isolated polypeptide comprising amino acid residues at least 90% identical to amino acids 60-240 of (S1), and STA;

(5) a composition (III) comprising a first **therapeutic** agent comprising an isolated polypeptide comprising amino acid residues at least 90% identical to amino acid residues 83-240 of (S1), and STA;

(6) a composition comprising (I), and a carrier;

(7) an isolated **antibody** (IV) which binds to a

polypeptide consisting of amino acid residues 1-208 of a fully defined sequence (S2) of 208 amino acids as given in specification;

(8) a composition (V) comprising (IV), and a carrier;

(9) an isolated **antibody** (VI) which binds to a polypeptide consisting of amino acid residues 1-240 of (S1);

(10) a composition (VII) comprising (VI), and a carrier;

(11) an isolated **antibody** (VIII) which binds to a polypeptide consisting of amino acid residues chosen from amino acids 13-20, 23-36, 69-79, 85-94, 167-178, 184-196 and 221-233 of (S1); and

(12) a composition (IX) comprising (VIII), and a carrier.

ACTIVITY - Cytostatic; Immunosuppressive; Neuroprotective; Antidiabetic; Antirheumatic; Antiarthritic; Hepatotrophic; Antianemic; Dermatological; Antiinflammatory; Hemostatic.

MECHANISM OF ACTION - Agonist or antagonist of AIM II polypeptide; Immunostimulant.

The inhibitory activity of TR6-(His) on AIM II polypeptide was determined in vitro. TR6-(His) a new member of tumor necrosis factor (TNF) superfamily was incubated overnight with various Flag-tagged ligands of TNF superfamily and anti-Flag agarose in binding buffer at 4 deg. C, and then precipitated. The bound proteins were resolved by 12.5% sodium dodecyl sulfate (SDS)-polyacrylamide gel electrophoresis (PAGE) and detected by Western blot with Horseradish peroxidase (HRP)-conjugated anti-poly(His)6 or anti-human IgG1 **antibodies**. For cell-binding assays, HEK 293 EBNA cells were stably transfected using calcium phosphate with pCEP4/full sequence of AIM II (LIGHT) cDNA or pCEP4 vector alone. After selection with Hygromycin B, cells were harvested with 1 mM EDTA in phosphate buffered saline (PBS) and incubated with TR6-(His), Herpes virus entry mediator (HVEM)/TR2-Fc, or **LT beta R**-Fc for 20 minutes on ice.
For detecting Fc-fusion protein, cells were stained with fluorescein isothiocyanate (FITC)-conjugated goat anti-human IgG. The cells were analyzed by FACScan. Cytotoxicity assays using HT29 cells were carried out.

Briefly, 5000 HT29 cells were seeded in 96-well plates with 1% fetal bovine serum (FBS), Dulbecco's modified eagle medium (DMEM) and **treated** with sAIM II (sLIGHT) (10 ng/ml) and 10 units/ml human recombinant interferon- gamma (IFN- gamma). Serial dilutions of TR6-(His) were added in quadruplicate to microtiter wells. Cells **treated** with IFN- gamma and sAIM II (sLIGHT) were incubated with various amounts of TR6-(His) for 4 days before the addition of (3H)thymidine for the last 6 hours of culture. Cells were harvested, and thymidine incorporation was determined using a liquid scintillation counter. TR6-(His) blocked nearly the entire AIM II (LIGHT)-mediated cell killing. Cells were also incubated with sAIM II (sLIGHT) and/or IFN- gamma in the presence of varying concentration of TR6-(His). TR6-(His) blocked sAIM (sLIGHT)-induced cell death dose-dependently. From these results, it was observed that TR6 acts as a natural inhibitor of AIM II (LIGHT)-induced tumor cell death and contributes to immune evasion by tumors.

USE - (II) is useful for **treating** an individual having a disorder chosen from graft versus host disease, immunodeficiency and autoimmunity, which involves administering (II) to the individual. (III) is useful for **treating** an individual having a disorder chosen from immunodeficiency and cancer, which involves administering (III) to the individual. (IV)-(IX) are useful for **treating** an autoimmune or a graft versus host disease in an individual, which involves administering any one of (IV)-(IX) to the individual (claimed).

(I) is useful for **preventing, treating,**

ameliorating, diagnosing or prognosing autoimmune diseases such as multiple sclerosis, type I diabetes, rheumatoid arthritis, primary biliary cirrhosis, aplastic anemia, myelodysplasia, systemic lupus erythematosus and idiopathic thrombocytopenic purpura.

(I) is useful for screening or identifying compounds capable of enhancing or inhibiting cellular response induced by AIM II, for inhibiting, blocking or reducing T-cell activation. (I) is useful as a molecular weight marker on SDS-PAGE gels or on gel filtration columns.

DESCRIPTION OF DRAWING(S) - The figure shows graphs representing the effect of Apoptosis inducing molecule II polypeptide on in vitro proliferation of human breast cancer cells.

Dwg.4/24

L31 ANSWER 9 OF 44 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2004624711 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15561941
TITLE: Absence of lymph nodes in NOD mice treated with lymphotoxin-beta receptor immunoglobulin protects from diabetes.
AUTHOR: Levisetti Matteo G; Suri Anish; Frederick Katherine; Unanue Emil R
CORPORATE SOURCE: Department of Medicine, Washington University School of Medicine, St. Louis, Missouri, USA.
SOURCE: Diabetes, (2004 Dec) 53 (12) 3115-9.
Journal code: 0372763. ISSN: 0012-1797.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 20041220
Last Updated on STN: 20050415
Entered Medline: 20050414

AB Pregnant nonobese diabetic (NOD) mice were **treated** with **lymphotoxin-beta receptor** immunoglobulin fusion protein (LTbetaR-Ig) or control human immunoglobulin on days embryonic day 11 (E11) and E14, and offspring were followed for the development of anti-beta-cell **antibodies**, islet pathology, and hyperglycemia. The development of anti-beta-cell surface **antibodies** was abrogated in **treated** mice compared with controls. Autopsy examination of the mice at 30 weeks of age revealed normal development of secondary lymphoid structures in the control animals; however, mice **treated** with LTbetaR-Ig had no axillary, inguinal, popliteal, or peripancreatic lymph nodes. Histological examination of the pancreata of the control mice revealed a severe and destructive mononuclear cellular infiltrate in the islets, whereas the islets of the LTbetaR-Ig-**treated** mice were devoid of any insulitis. None of the LTbetaR-Ig-**treated** mice (n = 22) developed diabetes; in contrast, 80% of the control mice (n = 46) developed diabetes at 1 year of age. The LTbetaR-Ig-**treated** mice did not contain diabetogenic T-cells. However, the **treated** mice developed diabetes upon inoculation with diabetogenic T-cells. In this model of spontaneous autoimmune diabetes, secondary lymphoid structures, most likely the peripancreatic lymph nodes, were essential for the development of pathologic anti-beta-cell autoimmunity.

L31 ANSWER 10 OF 44 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2004369541 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15240662
TITLE: Role of gut-associated lymphoreticular tissues in antigen-specific intestinal IgA immunity.
AUTHOR: Yamamoto Masafumi; Kweon Mi-Na; Rennert Paul D; Hiroi Takachika; Fujihashi Kohtaro; McGhee Jerry R; Kiyono Hiroshi
CORPORATE SOURCE: Department of Oral Medicine, Nihon University School of Dentistry, Matsudo, Chiba, Japan.. fumi@mascat.nihon-u.ac.jp
CONTRACT NUMBER: AI 18958 (NIAID)
AI 43197 (NIAID)
DE 12242 (NIDCR)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2004 Jul 15) 173 (2) 762-9.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 20040728
Last Updated on STN: 20040828
Entered Medline: 20040827

AB This study assessed the roles of the postnatal **lymphotoxin-beta receptor** (LTbetaR)-mediated signals in the gut-associated lymphoreticular tissues of mice for subsequent regulation of Ag-specific intestinal IgA responses. Blockade of LTbetaR-dependent events by postnatal administration of the fusion protein of LTbetaR and IgG **Fc** (LTbetaR-**Ig**) reduced both the size and numbers of Peyer's patches (PP) without influencing the PP microarchitecture. Interestingly, inhibition of LTbetaR-dependent signaling revealed significant reductions in the formation of follicular dendritic cell clusters in mesenteric lymph nodes (MLN). Furthermore, these postnatal signaling events controlled the development of isolated lymphoid follicles (ILF) because **treatment** with LTbetaR-Ig eliminated the formation of ILF. LTbetaR-Ig-**treated** mice with altered microarchitecture of MLN and lacking ILF were still able to produce significant Ag-specific mucosal IgA responses after oral immunization; however, the levels were significantly lower than those seen in control mice. These results imply the importance of ILF for Ag-specific intestinal immunity. However, mice **treated** with both TNFR55-Ig and LTbetaR-Ig in utero, which lack PP and MLN, but retain intact ILF, failed to induce Ag-specific IgA responses after oral immunization. These findings demonstrate that ILF are not essential for induction of intestinal IgA Ab responses to orally administered Ag. Furthermore, the induction of intestinal IgA Ab responses requires the proper maintenance of the MLN microarchitecture, including a follicular dendritic cell network.

L31 ANSWER 11 OF 44 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:170500 TOXCENTER
COPYRIGHT: Copyright 2005 ACS
DOCUMENT NUMBER: CA141111172737S
TITLE: Blocking of lymphotoxin-β receptor pathway in chronic colitis causes downregulation of MadCAM-1 and reduced leukocyte-endothelial cell interaction
AUTHOR(S): Janotta, M.; Stopfer, P.; Maennel, D. N.; Hehlgans, T.; Hornung, M.; Geissler, E.; Schlitt, H. J.; Farkas,

S.
CORPORATE SOURCE: Klinik und Poliklinik fuer Chirurgie, Universitaet Regensburg, Germany.
SOURCE: Chirurgisches Forum fuer Experimentelle und Klinische Forschung, (2004) pp. 241-243.
CODEN: CFEKA7. ISSN: 0303-6227.
COUNTRY: GERMANY, FEDERAL REPUBLIC OF
DOCUMENT TYPE: Journal
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2004:597806
LANGUAGE: German
ENTRY DATE: Entered STN: 20040803
Last Updated on STN: 20050104

AB The **lymphotoxin**-β **receptor** (**LT.beta.R**) pathway is critical for maintenance of organized lymphoid structures and involved in development of colitis as shown in different mouse colitis models. Thus, the mechanisms by which **LT.beta.R** activation contributes to the pathol. the chronic form of DSS-colitis was investigated. Moreover, it was demonstrated that mucosal addressin cell adhesion mol.-1 (MadCAM-1), which is strongly expressed in inflamed intestinal mucosa, plays a significant role in development of chronic DSS-colitis. Acute colitis was induced in Balb/c mice (20 ± 0.4g; n = 10 per group) by oral administration of 5% dextran sodium sulfate (DSS) dissolved in drinking water for 4 cycles of **treatment**. Two weeks after completion of 4 cycles of DSS **treatment**, mice in the **therapy** group received 100 μg i.p. of a monoclonal **antibody** against **LT.beta.R** for 6 days. Mice of the control group received 100μg of an isotype **antibody**. To prepare mice for cell injection, a venous and arterial catheter was implanted in anesthetized animals. The colon was then mobilized and extriorized for in vivo microscopy. Leukocyte-endothelium interaction in collecting and postcapillary venules was visualized and quantified by epiillumination at a 680-fold magnification. For in vivo microscopy of the mucosa the colon was incised and leukocyte extravasation was calculated Then tissue was taken out for histol. and immunohistochem. tests. **Treatment** of chronic form of DSS-induced colitis with **LT.beta.R**-Ig significantly attenuated the development and histol. manifestation of the disease. The expression of the proinflammatory cytokines TNF, IL-1β and IL-6 was clearly reduced by **LT.beta.R**-Ig **treatment** in the chronic form of colitis. Moreover **LT .beta.R**-Ig **treatment** significantly downregulated MadCAM-1 expression, leading to reduced leukocyte endothelium interaction. Addnl., reduced extravasation of leukocytes to intestinal mucosa was observed MadCAM expression was semi-quant. detected by immunhistochem. The authors' results show, that **LT.beta.R** pathway inhibition leads to a downregulation of MadCAM-1 expression. This leads to a significant reduction of leukocyte-endothelium interaction, extravasation of lymphocytes and also to a better histol. score. This study verifies the pathophysiol. role of **LT.beta.R** pathway inhibition in the rise of inflammatory bowel disease, that is mediated by MadCAM-1.

L31 ANSWER 12 OF 44 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2004332628 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15236187

TITLE: Lymphotoxin beta receptor signaling induces the chemokine CCL20 in intestinal epithelium.
AUTHOR: Rumbo Martin; Sierro Frederic; Debard Nathalie; Kraehenbuhl Jean-Pierre; Finke Daniela
CORPORATE SOURCE: Swiss Institute for Experimental Cancer Research, Lausanne Branch, Epalinges, Switzerland.
SOURCE: Gastroenterology, (2004 Jul) 127 (1) 213-23. Journal code: 0374630. ISSN: 0016-5085.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 20040707
Last Updated on STN: 20040929
Entered Medline: 20040928

AB BACKGROUND & AIMS: The follicle-associated epithelium (FAE) that overlies Peyer's patches (PPs) exhibits distinct features compared with the adjacent villus epithelium. Besides the presence of antigen-sampling membranous M cells and the down-regulation of digestive functions, it constitutively expresses the chemokine CCL20. The mechanisms that induce FAE differentiation and CCL20 expression are poorly understood. The aim of this work was to test whether **lymphotoxin beta receptor** signaling (LTbetaR), which plays a central role in PPs' organogenesis, mediates CCL20 gene expression in intestinal epithelial cells. METHODS: CCL20, lymphotoxin beta (LTbeta) and LTbetaR expression were monitored during embryonic development by in situ hybridization of mouse intestine. The human intestinal epithelial cell line T84 was used to study CCL20 expression following LTalpha(1)/beta(2) stimulation. In vivo CCL20 expression following agonistic anti-LTbetaR **antibody treatment** was studied by laser microdissection and quantitative RT-PCR. RESULTS: CCL20 was expressed in the FAE before birth at the time when the first hematopoietic CD4(+)CD3(-) appeared in the PP anlage. LTbetaR was expressed in the epithelium during PP organogenesis, making it a putative target for LTalpha(1)beta(2)signals. In vitro, CCL20 was induced in T84 cells upon LTbetaR signaling, either using an agonistic ligand or anti-LTbeta receptor agonistic **antibody**. LTalpha(1)beta(2)-induced CCL20 expression was found to be NF-kappaB dependent. LTbetaR signaling up-regulated CCL20 expression in the small intestinal epithelium in vivo. CONCLUSIONS: Our results show that LTbetaR signaling induces CCL20 expression in intestinal epithelial cells, suggesting that this pathway triggers constitutive production of CCL20 in the FAE.

L31 ANSWER 13 OF 44 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:288935 BIOSIS
DOCUMENT NUMBER: PREV200400287692
TITLE: Differential TNFR and LT beta R regulation of High Endothelial Venule (HEV) Specific Genes.
AUTHOR(S): Liao, Shan [Reprint Author]; Lesslauer, Werner; Ruddle, Nancy H
CORPORATE SOURCE: Epidemiology and Public Health, Yale University School of Medicine, 60 College Street, New Haven, CT, 06520-8034, USA
shan.liao@yale.edu
SOURCE: FASEB Journal, (2004) Vol. 18, No. 4-5, pp. Abst.

332.1. http://www.fasebj.org/. e-file.
Meeting Info.: FASEB Meeting on Experimental Biology: Translating the Genome. Washington, District of Columbia, USA. April 17-21, 2004. FASEB.
ISSN: 0892-6638 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jun 2004
Last Updated on STN: 16 Jun 2004

AB HEVs are specialized lymph node blood vessels where lymphocyte trafficking occurs. Optimal HEV function may be regulated at the level of gene expression of glycoproteins (GlyCAM-1, MAdCAM-1), chemokines (SLC) and posttranslational modifying enzymes (FucTIV, FucTVII, and an HEV specific GlcNAc-6-sulfotransferase (HEC-6ST)). We have previously determined that **LTbR** signaling contributes to HEV and HEC6ST in LTb-/- and in RIPLTab transgenic mice. Both the classical and alternative NF-kB pathways have been implicated in **LTbR** signal transduction in fibroblasts and spleen cells. However, it was not clear whether LTab could directly stimulate endothelial cells and/or whether its effect was mediated through stromal cells, which in turn activate HEV gene expression. Endothelial cell lines, bEND.3 and SVEC, were adopted as an in vitro system to evaluate and compare **LTbR** and TNFR mediated signaling for endothelial and HEV specific genes. FACS analysis revealed **LTbR** surface expression on both cell lines. Several genes were differentially induced by **treatment** with **LTbR** agonistic **antibody** or TNF. The signaling pathways regulating gene expression also differed as revealed by **treatment** with kinase or NF-kB inhibitors. Therefore, LTab has the capacity to directly activate endothelial cells and the pathways and genes differ from those employed by TNF. Supported by NIH CA16885 and the Anna Fuller Fund for Cancer Research.

L31 ANSWER 14 OF 44 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-665560 [63] WPIDS
DOC. NO. CPI: C2003-180986
TITLE: A composition containing an immunosuppressive agent and a molecule which inhibits binding of Herpesvirus entry mediator to the tumor necrosis factor superfamily member LIGHT is useful to treat or prevent immune disorders.
DERWENT CLASS: B04 B05 D16
INVENTOR(S): FRASER, C C; HANCOCK, W
PATENT ASSIGNEE(S): (MILL-N) MILLENIUM PHARM INC; (FRAS-I) FRASER C C; (HANC-I) HANCOCK W
COUNTRY COUNT: 32
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1336619	A2	20030820	(200363)*	EN	52
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR					
US 2003215442	A1	20031120	(200377)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

EP 1336619	A2	EP 2003-3651	20030218
US 2003215442	A1 Provisional	US 2002-358463P	20020219
		US 2003-369300	20030219

PRIORITY APPLN. INFO: US 2002-358463P 20020219; US 2003-369300 20030219

AN 2003-665560 [63] WPIDS

AB EP 1336619 A UPAB: 20031001

NOVELTY - Use of a Herpesvirus entry mediator (HVEM)-LIGHT inhibitor and an immunosuppressive agent to prepare a pharmaceutical composition to treat or prevent an immune disorder, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) an isolated nucleic acid:

(a) having a nucleotide sequence at least 90 % identical to 1082 base pair sequence (S1), given in the specification or its complement;

(b) comprising at least 15 consecutive nucleotides of residues 1-424 of (S1) or its complement;

(c) encoding a polypeptide comprising a 276 amino acid sequence (S2), given in the specification;

(d) encoding a fragment of at least 12 consecutive amino acids of (S2); or

(e) encoding a naturally occurring allelic variant of (S2) where the nucleic acid hybridizes under stringent conditions with residues 1-424 of (S1);

(2) host cell containing the nucleic acid of (1);

(3) an isolated polypeptide (P1) which is:

(a) a fragment of at least 12 amino acids of residues 1-80 of (S2);

(b) a naturally occurring allelic variant of (S2);

(c) encoded by a nucleic acid which hybridizes under stringent conditions to residues 1-424 of (S1) or its complement; or

(d) encoded by a nucleic acid comprising a sequence at least 90 % identical to a nucleic acid consisting of residues 1-424 of (S1) or its complement

(4) an antibody which selectively binds to P1 and not to a polypeptide comprising a 283 amino acid sequence, given in the specification;

(5) producing P1 comprising culturing the host cell of (2).

USE - For the treatment of allografts rejection, particularly heart, kidney, liver, lung, pancreas, heart valve, endothelial cornea, eye lens or bone marrow tissue, or delayed hypersensitivity, graft versus host disease, a drug allergy, atrophic gastritis, thyroiditis, allergic encephalomyelitis, autoimmune hemolytic anemia, sympathetic opthalmia, systemic lupus erythematosus, rheumatoid arthritis, multiple sclerosis, asthma inflammatory bowel disease or myasthenia gravis.

Dwg.0/1

L31 ANSWER 15 OF 44 TOXCENTER COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2003:206877 TOXCENTER
COPYRIGHT:	Copyright 2005 ACS
DOCUMENT NUMBER:	CA139121737692
TITLE:	Composition and method for modulating an inflammatory response
AUTHOR(S):	Kuai, Jun; Wooters, Joseph L.; Nickbarg, Elliott B.; Qiu, Yongchang; Lin, Lih-ling
CORPORATE SOURCE:	ASSIGNEE: Wyeth, John, and Brother Ltd.

PATENT INFORMATION: WO 2003066834 A2 14 Aug 2003
SOURCE: (2003) PCT Int. Appl., 29 pp.
CODEN: PIXXD2.
COUNTRY: UNITED STATES
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2003:633902
LANGUAGE: English
ENTRY DATE: Entered STN: 20030819
Last Updated on STN: 20050412

AB The invention relates to compns. and methods comprising **lymphotoxin-beta receptor** (**LT.beta.R**) modulators, which activate or inhibit **LT.beta.R** signaling. **LT.beta.R** modulators are useful for **treating** lymphocyte-mediated immunol. diseases and cancer, and more particularly, for regulating mitochondrial-mediated apoptosis. This invention relates to soluble forms of the **LTβR** complex proteins that act as **LTβR** activating or inhibiting agents. This invention also relates to the use of soluble mols., directed against either the **LT.beta.R**, its ligands, LIGHT and LTβ1α2, or its intracellular binding partners, that function to regulate **LT.beta.R** signaling. A novel screening method for selecting soluble receptors, **antibodies** and other agents that modulate **LT.beta.R** signaling is provided.

L31 ANSWER 16 OF 44 JICST-EPlus COPYRIGHT 2005 JST on STN
ACCESSION NUMBER: 1040199508 JICST-EPlus
TITLE: Role of Signaling Pathways through Tumor Necrosis Factor Receptor and Lymphotoxin B Receptor on the Intestinal Mucosal Immunity
AUTHOR: UEHARA YASUTSUGU
CORPORATE SOURCE: Nihon Univ., Sch. of Dent. at Matsudo
SOURCE: Nichidai Koku Kagaku (Nihon University Journal of Oral Science), (2003) vol. 29, no. 4, pp. 179-186. Journal Code: Z0705A (Fig. 5, Ref. 28)
ISSN: 0385-0145
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New

AB In this study, we examined the effect of signaling pathways through TNF receptor (TNFR) and **lymphotoxin**-B **receptor** (**LT.BETA.R**) on the development of the gut-associated lymphoreticular tissues with subsequent antigen-specific intestinal IgA **antibody** responses. Progeny of mice **treated** with TNFR with molecular mass of 55-kDa (TNFR55) and IgG chimeric protein (TNFR55-Ig) possessed Peyer's patches as well as mesenteric lymph nodes (MLN). Further, intestinal mucosal IgA **antibody** responses to orally administered ovalbumin (OVA) were induced in those in utero fusion protein **treated** mice. In contrast, blockade of signaling pathways through **LT.BETA.R** by **treatment** with **LT.BETA.R** and IgG fusion protein (**LT.BETA.R**-Ig) in utero resulted in the lack of Peyer's patches but not MLN. However, significant levels of intestinal mucosal IgA **antibody**

responses were induced when the mice were orally immunized. These results indicate that Peyer's patches are not essential inductive tissues for induction of antigen-specific intestinal IgA **antibody** responses. Interestingly, when mice were **treated** with both TNFR55-Ig and **LTB**
R-Ig in utero, neither Peyer's patches nor MLN were developed. Further, oral immunization of those Peyer's patches and MLN deficient mice with OVA failed to induce OVA-specific intestinal IgA **antibody** responses. These results suggest that the signaling pathways through both TNFR55 and **LT.BETA.R**
were involved in the development of MLN. Further, MLN play important roles for the induction of intestinal mucosal immune responses after oral immunization. (author abst.)

L31 ANSWER 17 OF 44 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2003272564 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12799047
TITLE: A simple method for enriching populations of transfected CHO cells for cells of higher specific productivity.
AUTHOR: Brezinsky S C G; Chiang G G; Szilvasi A; Mohan S; Shapiro R I; MacLean A; Sisk W; Thill G
CORPORATE SOURCE: Biogen Inc., 14 Cambridge Center, Cambridge, MA 02142, USA.
SOURCE: Journal of immunological methods, (2003 Jun 1) 277 (1-2) 141-55.
Journal code: 1305440. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 20030612
Last Updated on STN: 20030723
Entered Medline: 20030722

AB To establish a simple and rapid method for the screening of stable recombinant Chinese hamster ovary (CHO) cell lines, we have developed a cell surface labeling technique using fluorescently tagged **antibodies** that bind to secreted target proteins at low temperature. Using fluorescence intensity as the sole criterion for selection of cells, we are able to enrich populations of highly productive cells using preparative flow cytometry sorting. Reiterative sorting based on selection of cells having the highest fluorescence intensity of cell surface labeled protein results in dramatic increases in specific cellular productivity. Using **lymphotoxin-beta receptor** IgG fusion
protein as a model system, we have demonstrated a greater than 20-fold increase in specific productivity (0.49-11.5 pg cell(-1) day(-1)) (pcd) without the use of methotrexate (MTX)-mediated selection or amplification. In addition, the flow cytometry used to enrich for and clone high producer cell lines has reduced development time by more than 50% and the number of screening assays by more than 10-fold. When a transfected population of CHO cells expressing a humanized version of the murine monoclonal **antibody** (mAb) AQC2
directed against human alpha 1 beta 1 integrin was subjected to the same **treatment**, a 25-fold improvement in specific productivity (0.3-8.0 pcd) was observed. Furthermore, similar application of this technique to MTX-amplified clones resulted in up to 120-fold overall improvement in specific productivity (up to 42

pcd). Greater than 20 examples are also presented to demonstrate the robustness and performance of this technique.

L31 ANSWER 18 OF 44 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2003044946 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12554356
TITLE: Methotrexate stimulates lung epithelial cells to release inflammatory cell chemotactic activities.
AUTHOR: Koyama Sekiya; Sato Etsuro; Takamizawa Akemi; Tsukadaira Akihiro; Haniuda Masayuki; Kurai Makoto; Numanami Hiroki; Nagai Sonoko; Izumi Takateru
CORPORATE SOURCE: The National Chuushin Matsumoto Hospital, Matsumoto, Japan.. yskoyama@go.tvm.ne.jp
SOURCE: Experimental lung research, (2003 Mar) 29 (2) 91-111. Journal code: 8004944. ISSN: 0190-2148.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 20030130
Last Updated on STN: 20030822
Entered Medline: 20030821

AB Methotrexate-induced pneumonitis has been reported as an infrequent but potentially serious complication of **therapy** in a variety of malignant and benign conditions. Because inflammatory cell infiltration is concerned with the development of methotrexate-induced pneumoinitis, and because airway epithelial cells participate in the orchestration of lung inflammation, the authors determined whether methotrexate might stimulate airway epithelial cells (A549 cells) to release neutrophil, monocyte, and eosinophil chemotactic activities (NCA, MCA, and ECA). A549 cells released NCA, MCA, and ECA in a dose- and time-dependent manner in response to methotrexate. Partial characterization revealed the heterogeneity of NCA, MCA, and ECA. The release of chemotactic activity was blocked by lipoxygenase inhibitors and cycloheximide. NCA was inhibited by leukotriene (**LT**) **B**(4) **receptor** antagonist, and anti-interleukin (IL)-8 and granulocyte colony-stimulating factor (G-CSF) **antibodies**. MCA was attenuated by LTB(4) receptor antagonist, and anti-monocyte chemoattractant protein (MCP)-1 and granulocyte-macrophage CSF (GM-CSF) **antibodies**. ECA was attenuated by LTB(4) receptor antagonist, and anti-IL-8 and GM-CSF **antibodies**. The release of IL-8, G-CSF, MCP-1, GM-CSF, and LTB(4) from A549 cells significantly increased in response to methotrexate. The mRNA expression of IL-8 and MCP-1 was augmented by methotrexate stimulation. These data suggest that type II epithelial cells may modulate inflammatory cell recruitment into the lung by releasing NCA, MCA, and ECA in response to methotrexate.

L31 ANSWER 19 OF 44 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 10
ACCESSION NUMBER: 2002:389234 BIOSIS
DOCUMENT NUMBER: PREV200200389234
TITLE: Soluble lymphotoxin-beta receptors as therapeutic agents for the treatment of immunological disease.
AUTHOR(S): Browning, Jeffrey L. [Inventor, Reprint author]; Benjamin, Christopher D. [Inventor]; Hochman, Paula S. [Inventor]
CORPORATE SOURCE: Brookline, MA, USA

ASSIGNEE: Biogen, Inc., Cambridge, MA, USA
PATENT INFORMATION: US 6403087 20020611
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (June 11, 2002) Vol. 1259, No. 2. http://www.uspto.gov/web/menu/patdata.html. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Jul 2002
Last Updated on STN: 17 Jul 2002

AB This invention relates to compositions and methods comprising "**lymphotoxin-beta receptor** blocking agents", which block **lymphotoxin-beta receptor** signalling. **Lymphotoxin-beta receptor** blocking agents are useful for **treating** lymphocyte-mediated immunological diseases, and more particularly, for inhibiting Th1 cell-mediated immune responses. This invention relates to soluble forms of the **lymphotoxin-beta receptor** extracellular domain that act as **lymphotoxin -beta receptor** blocking agents. This invention also relates to the use of **antibodies** directed against either the **lymphotoxin-beta receptor** or its ligand, surface lymphotoxin, that act as **lymphotoxin-beta receptor** blocking agents. A novel screening method for selecting soluble receptors, **antibodies** and other agents that block **LT-beta receptor** signalling is provided.

L31 ANSWER 20 OF 44 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
DUPLICATE 11
ACCESSION NUMBER: 2002-583337 [62] WPIDS
DOC. NO. CPI: C2002-164764
TITLE: New humanized anti-**lymphotoxin-beta receptor antibody**, useful for **treating** or reducing the advancement, severity or effects of neoplasia, particularly solid tumors (i.e. carcinomas) including colorectal cancer and breast cancer.
DERWENT CLASS: B04 D16
INVENTOR(S): GARBER, E; LYNE, P; SALDANHA, J W; GARBER, E A
PATENT ASSIGNEE(S): (BIOJ) BIOGEN INC; (GARB-I) GARBER E; (LYNE-I) LYNE P; (SALD-I) SALDANHA J W
COUNTRY COUNT: 98
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002030986	A2	20020418	(200262)*	EN	40
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2002011747	A	20020422	(200269)		
EP 1326897	A2	20030716	(200347)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL					

	PT	RO	SE	SI	TR		
NO	2003001642		A	20030613	(200351)		
KR	2003041164		A	20030523	(200361)		
SK	2003000567		A3	20031007	(200369)		
CZ	2003001307		A3	20031015	(200374)		
HU	2003002573		A2	20031028	(200379)		
US	2004058394		A1	20040325	(200422)		
JP	2004532608		W	20041028	(200471)		80
ZA	2003003347		A	20050126	(200513)		65
CN	1547590		A	20041117	(200516)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2002030986	A2		WO 2001-US32140	20011012
AU 2002011747	A		AU 2002-11747	20011012
EP 1326897	A2		EP 2001-979824	20011012
			WO 2001-US32140	20011012
NO 2003001642	A		WO 2001-US32140	20011012
			NO 2003-1642	20030410
KR 2003041164	A		KR 2003-705232	20030414
SK 2003000567	A3		WO 2001-US32140	20011012
			SK 2003-567	20011012
CZ 2003001307	A3		WO 2001-US32140	20011012
			CZ 2003-1307	20011012
HU 2003002573	A2		WO 2001-US32140	20011012
			HU 2003-2573	20011012
US 2004058394	A1	Provisional	US 2000-240285P	20001013
		Provisional	US 2001-275289P	20010313
		Provisional	US 2001-299987P	20010621
		Cont of	WO 2001-US32140	20011012
			US 2003-412406	20030410
JP 2004532608	W		WO 2001-US32140	20011012
			JP 2002-534371	20011012
ZA 2003003347	A		ZA 2003-3347	20030430
CN 1547590	A		CN 2001-820591	20011012

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2002011747	A	Based on	WO 2002030986
EP 1326897	A2	Based on	WO 2002030986
SK 2003000567	A3	Based on	WO 2002030986
CZ 2003001307	A3	Based on	WO 2002030986
HU 2003002573	A2	Based on	WO 2002030986
JP 2004532608	W	Based on	WO 2002030986

PRIORITY APPLN. INFO: US 2001-299987P 20010621; US 2000-240285P 20001013; US 2001-275289P 20010313; US 2003-412406 20030410

AN 2002-583337 [62] WPIDS

AB WO 200230986 A UPAB: 20030111

NOVELTY - A new humanized anti-**lymphotoxin-beta receptor** (**LT- beta -R**) **antibody** (Ab1) whose light chain complementary determining regions (CDRs) are defined by amino acid residues 24-34, 50-56 and

89-97 of the 107 amino acid sequence (I) defined in the specification, and whose heavy chain CDRs are defined by residues 31-35, 50-66, and 99-109 of the 120 amino acid sequence (II) defined in the specification.

DETAILED DESCRIPTION - A new humanized anti-**lymphotoxin -beta receptor** (**LT- beta -R**) **antibody** (Ab1) whose light chain complementary determining regions (CDRs) are defined by amino acid residues 24-34, 50-56 and 89-97 of the 107 amino acid sequence (I) defined in the specification, and whose heavy chain CDRs are defined by residues 31-35, 50-66, and 99-109 of the 120 amino acid sequence (II) defined in the specification.

Ab1 comprises at least one of the following residues in its light chains: K3, W41, I46, Q69 and Y71.

Ab1 comprises at least one of the following residues in its heavy chains: F37, T40, A49, M89 and V93 (Kabat numbering convention).

INDEPENDENT CLAIMS are also included for the following:

(1) an **antibody** (Ab2) comprising the same heavy and light chain polypeptide sequences as an **antibody** produced by cell line E46.4 (ATCC patent deposition designation PTA-3357) or cell line E77.4 (ATCC patent deposit designation 3765);

(2) a method of **treating** or reducing the advancement, severity or effects of neoplasia in a human comprising administering a composition comprising Ab1 or Ab2;

(3) an isolated nucleic acid comprising a coding sequence for the light chain or heavy chain of an **antibody** produced by cell line E46.4 (ATCC patent deposition designation PTA-3357) or cell line E77.4 (ATCC patent deposit designation 3765);

(4) an isolated nucleic acid comprising a coding sequence for residues 1-107 of the other 107 amino acid sequence (III) defined in the specification;

(5) an isolated nucleic acid comprising a coding sequence for residues 1-120 of the other 120 amino acid sequence (IV) defined in the specification; and

(6) a cell line E46.4 (ATCC patent deposition designation PTA-3357) or cell line E77.4 (ATCC patent deposit designation 3765).

ACTIVITY - Cytostatic.

106 WIDR cells were pre-grown subcutaneously for 10 days in Nude mice. The mice received subcutaneous injections of either phosphate buffered saline (PBS) or huCBE11-4 (humanized anti-**LT-beta -R antibody** comprising version 3 (sequence of (III)) of the light chain and version 4 (sequence of (IV)) of the heavy chain) weekly or murine CBE11 (mCBE11) alternate weeks. Tumor weights were calculated from width and length measurements and animals with tumors over 2000 mg were sacrificed, their tumor weights at time of sacrifice continued into the statistical averaging. Tumor weights were calculated using the formula: (Width x Width x Length)/2= tumor weight in mg.

The results show that huCBE11-4 was able to slow pre-grown tumors in vivo as its dosage was increased compared to the control.

In addition, tumors were grown and **treated** as described above and percent survival of the animals was measured. The results show that huCBE11-4 was able to induce prolonged survival in vivo (90% of 500 microgram huCBE11-4 **treated** mice survived after 60 days post **treatment**) in mice with pre-grown tumors.

MECHANISM OF ACTION - The humanized anti-**LT-beta -R antibodies** activate the **lymphotoxin-beta receptor** (**LT-beta -R**) which in turn induces the apoptotic death

of the cancer cell.
USE - The humanized anti-**LT- beta -R** **antibodies** are useful for **treating** or reducing the advancement, severity or effects of neoplasia in a human. Preferably, the **antibodies** are used to **treat** solid tumors (i.e. carcinomas) including non-small cell lung cancer (NSCLC), colorectal cancer (CRC), breast cancer, as well as cancers of the prostate, gastric, skin, stomach, esophagus and bladder.
Dwg.0/8

L31 ANSWER 21 OF 44 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-615140 [71] WPIDS
DOC. NO. CPI: C2001-184131
TITLE: Production of anti-LTbetaR mAbs using recombinant LT-betaR.Fc fusion protein antigens.
DERWENT CLASS: B04 D16
INVENTOR(S): SHIE, S
PATENT ASSIGNEE(S): (NASC-N) NAT SCI COUNCIL
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
TW 434316	A	20010516	(200171)*		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
TW 434316	A	TW 1998-113614	19980819

PRIORITY APPLN. INFO: TW 1998-113614 19980819
AN 2001-615140 [71] WPIDS
AB TW 434316 A UPAB: 20011203
NOVELTY - Production of anti-LTbetaR monoclonal **antibodies** (mAb) using recombinant LT-betaRc fusion protein antigens, is new. Clone 25A8 is agonistic, while clone 1B8 is antagonistic mAb.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) production of LT beta Rc fusion gene by the ligation of extracellular domain of human **LT beta R** with the portion of human IgG1, then expressed either by baculovirus system or CHO (Chinese hamster ovary) cells;
(2) using the LT beta Rc fusion protein as antigen to obtain monoclonal **antibodies** against **LT beta R**. In conjunction with interferon-gamma, clone 25A8 could induce apoptosis (or programmed cell death) in several tumor cell lines, therefore it could be used for anti-cancer **therapy**.
The LT beta Rc fusion protein could be used to purify soluble form lymphotoxin alpha 1 beta 2 or alpha 1 beta 1 heterotrimer, or lymphotoxin alpha 1 beta 2, alpha 1 beta 1 or lymphotoxin alpha /LIGHT in vivo. **Antibody** generated against the recombinant LT alpha Rc fusion protein produced by baculovirus system can recognize the three-dimension epitope of human **LT beta R** . This will ensure the binding specificity to **antibody** to the native form of human **LT beta R**. The approach could be applied to other receptors whose extracellular domain is located on the N-terminal region.

Dwg.1/1

L31 ANSWER 22 OF 44 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:940016 SCISEARCH
THE GENUINE ARTICLE: 491RE
TITLE: **Lymphotoxin-beta receptor** agonist **antibodies** for **treatment** of cancer.
AUTHOR: Wilson C A (Reprint); Garber E; Bailly V; Ngam-Ek A; Ding J; Jarpe M; Lukashev M; Xu X; Browning J
CORPORATE SOURCE: Biogen Inc, Cambridge, MA 02142 USA
COUNTRY OF AUTHOR: USA
SOURCE: CLINICAL CANCER RESEARCH, (NOV 2001) Vol. 7, No. 11, Supp. [S], pp. 3786S-3786S. MA 661.
ISSN: 1078-0432.
PUBLISHER: AMER ASSOC CANCER RESEARCH, PO BOX 11806, BIRMINGHAM, AL 35202 USA.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0
ENTRY DATE: Entered STN: 7 Dec 2001
Last Updated on STN: 7 Dec 2001

L31 ANSWER 23 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 12
ACCESSION NUMBER: 2001107567 EMBASE
TITLE: Defective lymphotoxin-β receptor-induced NF-κB transcriptional activity in NIK-deficient mice.
AUTHOR: Yin L.; Wu L.; Wesche H.; Arthur C.D.; White J.M.; Goeddel D.V.; Schreiber R.D.
SOURCE: Science, (16 Mar 2001) Vol. 291, No. 5511, pp. 2162-2165.
Refs: 26
ISSN: 0036-8075 CODEN: SCIEAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20010503
Last Updated on STN: 20010503

AB The role of NF-κB-inducing kinase (NIK) in cytokine signaling remains controversial. To identify the physiologic functions of NIK, we disrupted the NIK locus by gene targeting. Although NIK(-/-) mice displayed abnormalities in both lymphoid tissue development and **antibody** responses, NIK(-/-) cells manifested normal NF-κB DNA binding activity when **treated** with a variety of cytokines, including tumor necrosis factor (TNF), interleukin-1 (IL-1), and lymphotoxin-β (LTβ). However, NIK was selectively required for gene transcription induced through ligation of **LTβ receptor** but not TNF receptors. These results reveal that NIK regulates the transcriptional activity of NF-κB in a receptor-restricted manner.

L31 ANSWER 24 OF 44 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:250089 BIOSIS
DOCUMENT NUMBER: PREV200200250089
TITLE: LIGHT, a TNF family member enhances the antigen presenting capacity of chronic lymphocytic leukemia cells and stimulates autologous cytolytic T-cells.
AUTHOR(S): Tolba, Khaled A. [Reprint author]; Bowers, William J.; Eling, David; Casey, Ann E.; Kipps, Thomas J.; Federoff, Howard J.; Rosenblatt, Joseph D.
CORPORATE SOURCE: James P Wilmot Cancer Center, University of Rochester, Rochester, NY, USA
SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 730a-731a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Apr 2002
Last Updated on STN: 24 Apr 2002

AB Members of the TNF superfamily play a key role in immune regulation and activation of effector cells, an activity that has been extended to generate anti-tumor immune response both in vitro and in vivo, (CD40/CD40L, 4-1-BB/4-1BBL and OX-40/OX-40L). LIGHT, (TNFSF14) a recently cloned member of the TNF superfamily binds Hve-A (formerly known as HVEM), **lymphotoxin beta receptor** (LTbetaR) and DcR3/TR6. Signaling through the Hve-A receptor activates both the T-cell and antigen presenting cell (APC) through recruitment of members of the TRAF family of adaptor molecules that will eventually activate the NF-kappaB and AP-1 transcription factors, while binding the LTbetaR induces apoptosis in several tumor cell lines. The cDNA for human LIGHT was cloned by RT-PCR from dendritic cell mRNA, subcloned into an HSV amplicon plasmid and packaged using helper virus-free methodology. The packaged vector, hf-HSV-LIGHT, was used to transduce human chronic lymphocytic leukemia (CLL) cells. Expression of LIGHT on CLL cells was detected by flow-cytometry using both a soluble Hve-A/Fc fusion protein and anti-LIGHT monoclonal **antibody**. We studied the immune modulatory function and T-cell activation by LIGHT in comparison to CD40L, both delivered using helper-free HSV amplicon vectors. LIGHT expression induced up-regulation of B7.1, B7.2 and ICAM.1 on CLL cells, albeit to a lesser degree than seen in response to transduced CD40L. LIGHT expression enhanced antigen presenting capacity of the transduced CLL cells as shown in an allogeneic mixed lymphocyte tumor reaction (MLTR). Hf-HSV-LIGHT transduced CLL cells successfully stimulated the generation of specific autologous cytotoxic T-lymphocyte activity following in vitro priming. CTL activity was blocked by the anti-MHC-I **antibody** W6-32. Our data suggests that expression of LIGHT using an HSV amplicon vector may be a useful strategy for immune **therapy** of B-cell lymphoid malignancies and CLL gene **therapy**.

L31 ANSWER 25 OF 44 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:291329 BIOSIS
DOCUMENT NUMBER: PREV200100291329
TITLE: Mesenteric lymph nodes but not Peyer's patches are critical for oral tolerance.

AUTHOR(S): Spahn, Thomas Werner [Reprint author]; Rennert, Paul D.; Weiner, Howard L.; Domschke, Wolfram [Reprint author]; Luegering, Norbert [Reprint author]; Kucharzik, Torsten
CORPORATE SOURCE: Westfaelische Wilhelms-Universitaet Muenster, Albert Schweitzer Str. 33, Muenster, 48161, Germany
SOURCE: FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A368. print.
Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001. Orlando, Florida, USA. March 31-April 04, 2001.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Jun 2001
Last Updated on STN: 19 Feb 2002

AB We have previously demonstrated deficient oral tolerance (OT) in TNFalpha/Lymphotoxinalpha knockout (TNFalpha/LTalpha-/-) mice without Peyer's patches (PP) and mesenteric lymph nodes (MLN). We have now studied OT in mice with differential defects of PP and MLNs caused by inhibition of Lymphotoxin receptor ligand interaction during pregnancy. **Treatment** of pregnant mice with **Lymphotoxin-beta-receptor**-IgG (LTbetaRIgG) and TNF-receptor-I(55)-IgG (TNFR55IgG) fusion proteins abrogates the formation of PPs (LTbetaRIgG alone) or of PPs and MLNs (combined **treatment**) without a simultaneous cytokine defect. Single feeding of 20 mg Ovalbumin (OVA) similarly induced oral tolerance in mice with a selective PP defect (PP-/LN+) and control mice, consistent with our previous observation of intact oral tolerance in LTbeta-/-mice and LTalpha/LTbeta+/-mice without PPs and with MLNs. Oral tolerance could not be induced in mice deficient of MLN and PPs (PP-/MLN-). Feeding of 20 mg or 200 mg OVA failed to suppress gamma-IFN secretion by splenocytes or delayed type hypersensitivity reactions in PP-/LN- mice while control mice were tolerized. However, intraperitoneal antigen induced peripheral tolerance in PP-/MLN- and control animals. Injection of TNFR55IgG and LTbetaRIgG in mice prior to oral tolerance induction did not abrogate oral tolerance. To further assess the role of MLN in oral tolerance we generated Lymphotoxinalpha-/- mice with MLN and without PPs. **Treatment** of pregnant LTalpha-/- mice with anti-LTalpha **antibody** AF.H6 induces formation of MLN but not of PP in LTalpha-/- mice congenitally devoid of MLN and PP. MLN+/PP- LTalpha-/- mice could be orally tolerized while untreated LTalpha-/- mice failed to induce tolerance following oral OVA. We conclude that mesenteric lymph nodes are critical for the induction of oral tolerance.

L31 ANSWER 26 OF 44 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-656167 [63] WPIDS
CROSS REFERENCE: 2000-664925 [64]
DOC. NO. CPI: C2000-198584
TITLE: FAS Ligand Inhibitory Protein analogs useful for treating abnormal apoptosis related diseases e.g. acute lung injury, pulmonary fibrosis, chronic obstructive pulmonary disease ulcerative colitis or Crohn's disease.
DERWENT CLASS: B04 D16
INVENTOR(S): BECKER, G W; COHEN, F J; GONZALEZ-DEWHITT, P A; HALE,

J E; MICANOVIC, R; NEWTON, C M; NOBLITT, T W; RATHMACHALAM, R; TSCHANG, S R; WITCHER, D R; WROBLEWSKI, V J

PATENT ASSIGNEE(S): (ELIL) LILLY & CO ELI
COUNTRY COUNT: 92
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000058465	A2	20001005	(200063)*	EN	114
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000037394	A	20001016	(200106)		
EP 1165780	A2	20020102	(200209)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2002539828	W	20021126	(200307)		112

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000058465	A2	WO 2000-US6417	20000320
AU 2000037394	A	AU 2000-37394	20000320
EP 1165780	A2	EP 2000-916263	20000320
		WO 2000-US6417	20000320
JP 2002539828	W	JP 2000-608746	20000320
		WO 2000-US6417	20000320

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000037394	A	Based on	WO 2000058465
EP 1165780	A2	Based on	WO 2000058465
JP 2002539828	W	Based on	WO 2000058465

PRIORITY APPLN. INFO: US 2000-183398P 20000218; US 1999-126839P 19990330; US 1999-140077P 19990621; US 1999-140156P 19990621; US 1999-160566P 19991020

AN 2000-656167 [63] WPIDS
CR 2000-664925 [64]
AB WO 200058465 A UPAB: 20030129
NOVELTY - A FAS Ligand Inhibitory Protein (FLINT) analog comprising a modified form of a 271 residue amino acid sequence (S1), fully defined in the specification, or its fragment, having FLINT biological activity, is new.

DETAILED DESCRIPTION - A FAS Ligand Inhibitory Protein (FLINT) analog comprising a modified form of a 271 residue amino acid sequence (S1), fully defined in the specification, or its fragment, having FLINT biological activity, is new. (I) comprises the substitution:

(a) Trp to Asp at position 53, Thr to Pro at position 88, Ala to Ser, Glu or Thr at position 107, Ile to Thr or Glu at position 110 or

Pro to Ser at position 104;

(b) Ala to Asn at position 2 or 12, Pro to Asn at position 25, 38, 126 or 171, Arg to Asn at position 35, Ser to Asp at position 37 and Pro to any amino acid at position 38, Ser to Asn at position 166, Leu to Asn at position 172, Asp to Asn at position 194 or Thr to Asn at position 114 and Pro to any amino acid at position 115;

(c) Asn to Trp at position 63, Gly to Asp at position 67 and Ala at position 94 or Gly at position 95 to Tyr, Arg to Glu at position 69, Arg to Glu or Thr at position 82, Ala to Tyr at position 94 and Gly to Asp at position 95, Phe to Glu at position 96, Ala to Thr at position 101, or Gly to Asp at position 95;

(d) Arg to Glu, Asn, Ser or Thr at position 10, where if the substitution is to Asn then Ala is substituted by Ser or Thr at position 12, Glu to Gln, Asn, Ser or Thr at position 13, where if the substitution is to Asn then Gly is substituted by Ser or Thr at position 15, Glu to Gln, Asn, Ser, or Thr at position 16, where if the substitution is to Asn then Leu is substituted by Ser or Thr at position 18, Arg to Gln, Asn, Ser or Thr at position 17, where if the substitution is to Asn then Val is substituted by Ser or Thr at position 19, Arg to Gln, Asn, Ser or Thr at position 17, where if the substitution is to Asn then Cys is substituted by Ser or Thr at position 33, Arg to Gln, Asn, Ser or Thr at position 34, where if the substitution is to Asn then Asp is substituted by Ser or Thr at position 36, Arg to Gln, Asn, Ser or Thr at position 35, Asp to Gln, Asn, Ser or Thr at position 36, where if the substitution is to Asn then Pro is substituted by Ser or Thr at position 38, Arg to Gln, Asn, Ser or Thr at position 143, where if the substitution is to Asn then Cys is substituted by Ser or Thr at position 145, or Asp to Gln, Asn, Ser or Thr at position 161, where if the substitution is to Asn then Leu is substituted by Ser or Thr at position 163;

(e) Ala to Thr position 2, 12,107, 179 or 209, Thr to Ala at position 4 or 162, Val at position 1, or Ile at position 110 to Met; Glu to Asp at position 13, Arg to Trp at position 17, Ala to Pro at position 75, Ser to Leu at position 102, Gly to Ala at position 169, Glu to Lys at position 183, Gln to Arg at position 225, Gly to Glu at position 237, or Val to Gly at position 270; or

(f) Ala to Asn at position 12 and Glu to Gln at position 13, Arg to Asn at position 34 and Asp to Thr at position 36, Arg to Asp at position 35 and Ser to Thr at position 37, Ser to Asn at position 132 and Ser to Thr at position 134, Asp to Asn at position 194 and Ser to Thr at position 196, Arg at position 35 and Asp at position 194 to Asn, Ala to Asn at position 12 Glu to Gln at position 13 Asp to Asn at position 194 and Ser to Thr at position 194, Arg to Asp at position 34 Asp to Asn at position 194 and Ser to Thr at position 196, Arg at position 35 and Asp at position 194 to Asn and Ser to Thr at position 37 and/or 196, or Arg to Gln at position 218.

INDEPENDENT CLAIMS are also included for the following:

(1) a polypeptide fragment (II) of FLINT which is biologically active in vivo or in vitro;

(2) a fusion protein having a formula (III) ;

(3) a nucleic acid (IV) encoding (I), (II) or the fusion protein;

(4) a polynucleotide (V) comprising (IV);

(5) a vector (VI) comprising (IV) or (V);

(6) a host cell transformed with (VI); and

(7) a pharmaceutical composition comprising (I).

Fc = Fc fragment of an **antibody**; and

X = independently, a peptide derivative of (I) or (II) or protease resistant FLINT analog.

X is covalently linked at its C terminus to the N terminus of Fc

fragment of the **antibody**.

ACTIVITY - Antiinflammatory; antiapoptopic; antiulcer; cytostatic. BALB/c mice were given intravenous injections in the lateral tail vein of 6 mg of D(+)- Galactosamine and 100 ml of phosphate buffer saline in 3 micro g of lipopolysaccharide (LPS) B Escherichia coli in 100 micro l of phosphate buffered saline (PBS). After LPS challenge, the animals were injected intraperitonially with (I) (200 micro g). Suitable controls included hamster immunoglobulin (Ig)G (500 micro g), monoclonal **antibody** (mAb) against murine tumor necrosis factor, TN3-19.12 and anti-mouse Fas Ligand at 0, 2, 4, 6 hour-point respectively. The survival rates of the mice were determined 24 and 48 hours after LPS injection. The results showed that FLINT analog was effective in protecting animals from acute liver damage.

MECHANISM OF ACTION - Inhibitor of binding of FasL to Fas or LIGHT to **LT beta R** and/or TR2/herpes virus entry mediator.

USE - (I) is useful for **treating** a patient suffering from disease or condition relating to abnormal apoptosis such as acute lung injury, acute respiratory distress syndrome, pulmonary fibrosis, chronic obstructive pulmonary disease, ulcerative colitis, or Crohn's disease.

Dwg.0/2

L31 ANSWER 27 OF 44 TOXCENTER COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2000:138978 TOXCENTER
COPYRIGHT:	Copyright 2005 ACS
DOCUMENT NUMBER:	CA13222292716V
TITLE:	Reversal of viral-induced systemic shock and respiratory distress by blockade of the lymphotoxin β pathway
AUTHOR(S):	Browning, Jeff; Puglielli, Maryann; Ahmed, Rafi
CORPORATE SOURCE:	ASSIGNEE: Biogen, Inc.
PATENT INFORMATION:	WO 2000021558 A1 20 Apr 2000
SOURCE:	(2000) PCT Int. Appl., 40 pp. CODEN: PIXXD2.
COUNTRY:	UNITED STATES
DOCUMENT TYPE:	Patent
FILE SEGMENT:	CAPLUS
OTHER SOURCE:	CAPLUS 2000:260054
LANGUAGE:	English
ENTRY DATE:	Entered STN: 20011116 Last Updated on STN: 20020416

AB This invention provides methods of inducing an antiviral response in an individual comprising administering to the individual an effective amount of a LT-β blocking agent and a pharmaceutically acceptable carrier. In particular this invention provides methods for **treating** viral-induced systemic shock and respiratory distress. The LT-β inhibitor is an anti-LT-β **antibody**, soluble **LT-β receptor**, or fusion protein containing **LT-β receptor** and Ig.

L31 ANSWER 28 OF 44 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER:	2001:2503 BIOSIS
DOCUMENT NUMBER:	PREV200100002503
TITLE:	Evaluation of the tumor necrosis factor (TNF) family of inhibitors in the dextran sulfate model of mouse

colitis.
AUTHOR(S): Murthy, S. [Reprint author]; Flanigan, A. [Reprint author]; Osborne, B. [Reprint author]
CORPORATE SOURCE: MCP Hahnemann University, Philadelphia, PA, USA
SOURCE: Digestive and Liver Disease, (May, 2000) Vol. 32, No. Supplement 1, pp. A20. print.
Meeting Info.: International Meeting on Inflammatory Bowel Diseases. Capri, Italy. June 18-21, 2000.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Dec 2000
Last Updated on STN: 21 Dec 2000

L31 ANSWER 29 OF 44 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:435938 BIOSIS
DOCUMENT NUMBER: PREV199900435938
TITLE: Soluble **lymphotoxin-beta receptors** and anti-lymphotoxin receptor and ligand **antibodies** as **therapeutic** agents for the **treatment** of immunological disease.
AUTHOR(S): Browning, Jeffrey L. [Inventor, Reprint author]; Benjamin, Christopher D. [Inventor]; Hochman, Paula S. [Inventor]
CORPORATE SOURCE: Slone Epidemiology Unit, School of Public Health, Boston University School of Medicine, Brookline, MA, USA
ASSIGNEE: Biogen, Inc.
PATENT INFORMATION: US 5925351 19990720
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Jul. 20, 1999) Vol. 1224, No. 3. print.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Oct 1999
Last Updated on STN: 18 Oct 1999

L31 ANSWER 30 OF 44 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 1999-469242 [39] WPIDS
DOC. NO. NON-CPI: N1999-350374
DOC. NO. CPI: C1999-137711
TITLE: New method of treating follicular lymphomas by inhibiting interaction between lymphotoxin-beta and its receptor.
DERWENT CLASS: B04 D16 P34
INVENTOR(S): BROWNING, J; THORBECKE, J; TSIAGBE, V
PATENT ASSIGNEE(S): (BIOJ) BIOGEN INC; (UYNY) UNIV NEW YORK SCHOOL MEDICINE; (UYNY) UNIV NEW YORK STATE
COUNTRY COUNT: 85
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9938525	A1	19990805	(199939)*	EN	31

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

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      W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB
         GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT
         LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ
         TM TR TT UA UG US UZ VN YU ZW
   AU 9923488      A  19990816 (200002)
   EP 1051187      A1 20001115 (200059)  EN
      R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL
         PT RO SE SI
   NO 2000003848   A  20001002 (200061)
   BR 9908214      A  20001128 (200067)
   CZ 2000002751   A3 20001213 (200103)
   SK 2000001130   A3 20010118 (200108)
   CN 1289252      A  20010328 (200140)
   KR 2001040497   A  20010515 (200167)
   HU 2001002363   A2 20011029 (200175)
   JP 2002501902   W  20020122 (200211)       36
   AU 752710       B  20020926 (200268)
   MX 2000007403   A1 20011001 (200274)
   NZ 506529       A  20021220 (200309)
   EP 1051187      B1 20031112 (200380)  EN
      R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL
         PT RO SE SI
   DE 69912743     E  20031218 (200407)
   ES 2211035      T3 20040701 (200444)
   EP 1051187      B9 20040811 (200452)  EN
      R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL
         PT RO SE SI
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APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9938525	A1	WO 1999-US1928	19990129
AU 9923488	A	AU 1999-23488	19990129
EP 1051187	A1	EP 1999-903480	19990129
		WO 1999-US1928	19990129
NO 2000003848	A	WO 1999-US1928	19990129
		NO 2000-3848	20000727
BR 9908214	A	BR 1999-8214	19990129
		WO 1999-US1928	19990129
CZ 2000002751	A3	WO 1999-US1928	19990129
		CZ 2000-2751	19990129
SK 2000001130	A3	WO 1999-US1928	19990129
		SK 2000-1130	19990129
CN 1289252	A	CN 1999-802490	19990129
KR 2001040497	A	KR 2000-708353	20000731
HU 2001002363	A2	WO 1999-US1928	19990129
		HU 2001-2363	19990129
JP 2002501902	W	WO 1999-US1928	19990129
		JP 2000-529257	19990129
AU 752710	B	AU 1999-23488	19990129
MX 2000007403	A1	MX 2000-7403	20000728
NZ 506529	A	NZ 1999-506529	19990129
		WO 1999-US1928	19990129
EP 1051187	B1	EP 1999-903480	19990129
		WO 1999-US1928	19990129
DE 69912743	E	DE 1999-612743	19990129
		EP 1999-903480	19990129
		WO 1999-US1928	19990129

Searcher : Shears 571-272-2528

ES 2211035	T3	EP 1999-903480	19990129
EP 1051187	B9	EP 1999-903480	19990129
		WO 1999-US1928	19990129

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9923488	A	Based on	WO 9938525
EP 1051187	A1	Based on	WO 9938525
BR 9908214	A	Based on	WO 9938525
CZ 2000002751	A3	Based on	WO 9938525
HU 2001002363	A2	Based on	WO 9938525
JP 2002501902	W	Based on	WO 9938525
AU 752710	B	Previous Publ.	AU 9923488
		Based on	WO 9938525
NZ 506529	A	Based on	WO 9938525
EP 1051187	B1	Based on	WO 9938525
DE 69912743	E	Based on	EP 1051187
		Based on	WO 9938525
ES 2211035	T3	Based on	EP 1051187
EP 1051187	B9	Based on	WO 9938525

PRIORITY APPLN. INFO: US 1998-73410P 19980202; US 1998-73112P 19980130

AN 1999-469242 [39] WPIDS

AB WO 9938525 A UPAB: 19990928

NOVELTY - A method for arresting or reducing, severity of effects of a tumor by administration of a composition which inhibits the interaction between lymphotoxin (LT)- beta and its receptor.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) A composition for the treatment of a subject having follicular lymphoma which blocks the interaction of LT- beta with its receptor;

(2) A method for altering the survival or maintenance of follicular dendritic cells in a subject by administering an inhibitor of the interaction between LT- beta and its receptor;

(3) A method for altering the architecture of the organs of the immune system by administering:

(a) an inhibitor of the interaction between LT- beta and its receptor; and

(b) an inhibitor of the signaling pathway of an additional member of the tumor necrosis factor (TNF) family of ligands and receptors.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - The composition blocks the interaction of the LT- alpha /b heteromer with its receptor.

USE - The method is useful for treating tumors, specifically follicular lymphomas. It offers an alternative therapy for those with tumors resistant to traditional chemotherapy.

Dwg.0/0

L31 ANSWER 31 OF 44 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 1999-120787 [10] WPIDS

CROSS REFERENCE: 2002-026029 [03]

DOC. NO. NON-CPI: N1999-088120

DOC. NO. CPI: C1999-035386

TITLE: New ligand for herpes virus entry mediator - used to develop products for treating e.g. autoimmune

disease, lymphomas, leukaemias, infections, immunosuppression or AIDS.

DERWENT CLASS: B04 D16 S03

INVENTOR(S): WARE, C F; WARE, C; WARE, C E

PATENT ASSIGNEE(S): (LJOL-N) LA JOLLA INST ALLERGY & IMMUNOLOGY; (WARE-I) WARE C

COUNTRY COUNT: 84

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9902563	A1	19990121	(199910)*	EN	60
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW					
AU 9882882	A	19990208	(199924)		
EP 1003782	A1	20000531	(200031)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
US 6140467	A	20001031	(200057)		
CN 1268953	A	20001004	(200067)		
JP 2001509373	W	20010724	(200147)		62
KR 2001021579	A	20010315	(200159)		
AU 741419	B	20011129	(200206)		
US 2003060605	A1	20030327	(200325)		
TW 222453	B1	20041021	(200532)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9902563	A1		WO 1998-US13897	19980707
AU 9882882	A		AU 1998-82882	19980707
EP 1003782	A1		EP 1998-933153	19980707
			WO 1998-US13897	19980707
US 6140467	A	Provisional	US 1997-51964P	19970707
			US 1997-898234	19970730
CN 1268953	A		CN 1998-808663	19980707
JP 2001509373	W		WO 1998-US13897	19980707
			JP 2000-502082	19980707
KR 2001021579	A		KR 2000-700137	20000107
AU 741419	B		AU 1998-82882	19980707
US 2003060605	A1	Provisional	US 1997-51964P	19970707
		CIP of	US 1997-898234	19970730
		CIP of	US 2000-549096	20000412
			US 2001-967604	20010928
TW 222453	B1		TW 1998-110978	19980707

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9882882	A	Based on	WO 9902563
EP 1003782	A1	Based on	WO 9902563
JP 2001509373	W	Based on	WO 9902563
AU 741419	B	Previous Publ.	AU 9882882
		Based on	WO 9902563

Searcher : Shears 571-272-2528

US 2003060605 A1 CIP of US 6140467

PRIORITY APPLN. INFO: US 1997-898234 19970730; US
1997-51964P 19970707; US
2000-549096 20000412; US
2001-967604 20010928

AN 1999-120787 [10] WPIDS
CR 2002-026029 [03]
AB WO 9902563 A UPAB: 20050520

The following are claimed: (1) a purified polypeptide characterised by: (a) having a molecular weight of 30 kDa as determined by SDS-PAGE; (b) a pI of about 7 to 8.5; (c) binding to the herpes virus entry mediator (HVEM) polypeptide; and (d) binding to the **lymphotoxin beta receptor** (**LT beta R**) polypeptide; (2) an isolated nucleic acid sequence which encodes a polypeptide as in (A); (3) an expression vector containing a nucleic acid sequence as in (2); (4) a host cell containing a expression vector as in (3); (5) an **antibody** that binds to a polypeptide as in (1); (6) identifying a compound which affects an HVEM-binding agent-mediated cellular response comprising: (a) incubating the compound with an HVEM polypeptide or a cell expressing an HVEM polypeptide, and an HVEM-binding agent, to allow the components to interact; and (b) determining the effect of the compound on the HVEM-binding agent-mediated cellular response; (7) identifying a compound which affects an **LT beta R**-p300-mediated cellular response, comprising: (a) incubating the compound with an **LT beta R** polypeptide or a cell expressing an **LT beta R** polypeptide, and with p30, to allow the components to interact; and (b) determining the effect of the compound on the **LT beta R**-p30-mediated cellular response; (8) modulating an HVEM-mediated cellular response, comprising contacting a cell expressing HVEM with an HVEM binding agent or a p30 binding agent; (9) modulating an HVEM-mediated cellular response comprising contacting a cell expressing the HVEM with an HVEM binding agent or an LT alpha binding agent; (10) modulating an **LT beta R**-mediated cellular response comprising contacting a cell expressing **LT beta R** with an **LT beta R** binding agent or a p30 binding agent, and (11) inhibiting herpes simplex virus (HSV) infection of a cell, comprising contacting a cell susceptible to HSV infection with a HVEM binding agent, to inhibit HSV infection.

USE - The novel 30 kDa polypeptide ligand, designated p30, can bind to HVEM and LT beta . The products can be used for detection, diagnosis and screening assays. Inhibitors of p30 or LT alpha interactions with HVEM, or p30 interactions with **LT beta R**, could be used to modulate diseases where unwanted lymphocytes proliferation occurs, including T and B lymphomas or leukaemias, or in autoimmune diseases such as rheumatoid arthritis, insulin-dependent diabetes mellitus, multiple sclerosis, systemic lupus erythematosus or myasthenia gravis. They can also be used to inhibit herpes virus infection by blocking the ability of herpes virus to enter a cellular target. Compounds which stimulate lymphocyte activation can be used for stimulating immune responses in subjects with infectious diseases, or in which the subject is immunosuppressed as, e.g. in patients undergoing chemotherapy or radiation **therapy** for cancer or in patients with AIDS.

Dwg.0/7

L31 ANSWER 32 OF 44 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
DUPLICATE 13
ACCESSION NUMBER: 1998-261192 [23] WPIDS
DOC. NO. CPI: C1998-081105
TITLE: Modulating humoral immune response by blocker of lymphotoxin beta receptor - useful for, e.g. treating graft rejection or infection by human immune deficiency virus, without affecting signalling through tumour necrosis factor receptor.
DERWENT CLASS: B04 D16
INVENTOR(S): BROWNING, J; HOCHMAN, P S; MACKAY, F; RENNERT, P D; BROWING, J; BROWNING, J L
PATENT ASSIGNEE(S): (BIOJ) BIOGEN INC; (BROW-I) BROWNING J L; (HOCH-I) HOCHMAN P S; (MACK-I) MACKAY F; (RENN-I) RENNERT P D
COUNTRY COUNT: 79
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9817313	A2	19980430	(199823)*	EN	77
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9850896	A	19980515	(199838)		
CZ 9901428	A3	19990714	(199933)		
NO 9901926	A	19990625	(199935)		
EP 954333	A2	19991110	(199952)	EN	
R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT RO SE SI					
BR 9712670	A	19991019	(200008)		
CN 1237910	A	19991208	(200016)		
HU 9904516	A2	20000528	(200035)		
SK 9900553	A3	20001009	(200056)		
NZ 335353	A	20000929	(200060)		
AU 726357	B	20001102	(200062)		
MX 9903801	A1	19990801	(200063)		
JP 2001502697	W	20010227	(200115)		71
KR 2000052800	A	20000825	(200121)		
US 2002197254	A1	20021226	(200304)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9817313	A2	WO 1997-US19436	19971024
AU 9850896	A	AU 1998-50896	19971024
CZ 9901428	A3	WO 1997-US19436	19971024
		CZ 1999-1428	19971024
NO 9901926	A	WO 1997-US19436	19971024
		NO 1999-1926	19990422
EP 954333	A2	EP 1997-913798	19971024
		WO 1997-US19436	19971024
BR 9712670	A	BR 1997-12670	19971024
		WO 1997-US19436	19971024
CN 1237910	A	CN 1997-199906	19971024
HU 9904516	A2	WO 1997-US19436	19971024

			HU 1999-4516	19971024
SK 9900553	A3		WO 1997-US19436	19971024
			SK 1999-553	19971024
NZ 335353	A		NZ 1997-335353	19971024
			WO 1997-US19436	19971024
AU 726357	B		AU 1998-50896	19971024
MX 9903801	A1		MX 1999-3801	19990423
JP 2001502697	W		WO 1997-US19436	19971024
			JP 1998-519688	19971024
KR 2000052800	A		WO 1997-US19436	19971024
			KR 1999-703619	19990424
US 2002197254	A1	Provisional	US 1996-29060P	19961025
		Cont of	US 1999-299139	19990423
			US 2001-3211	20011031

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9850896	A	Based on	WO 9817313
CZ 9901428	A3	Based on	WO 9817313
EP 954333	A2	Based on	WO 9817313
BR 9712670	A	Based on	WO 9817313
HU 9904516	A2	Based on	WO 9817313
NZ 335353	A	Based on	WO 9817313
AU 726357	B	Previous Publ.	AU 9850896
		Based on	WO 9817313
JP 2001502697	W	Based on	WO 9817313
KR 2000052800	A	Based on	WO 9817313

PRIORITY APPLN. INFO: US 1996-29060P 19961025

AN 1998-261192 [23] WPIDS

AB WO 9817313 A UPAB: 19980610

The humoral immune response in an animal is altered by administering an agent (I) that blocks the **lymphotoxin beta receptor** (**LT beta R**). Also claimed are compositions: (a) for **treating** graft rejection comprising (I) plus agent (II) that blocks CD40 ligand, and (b) for **treating** AIDS or HIV infection comprising azidothymidine (AZT), protease inhibitors and (I).

USE - (I) are particularly used to inhibit the human humoral response, to regulate expression of addressins and cell trafficking, and to modify differentiation of follicular dendritic cells (FDC). Particularly they alter association of immune complexes with B cell follicles (especially FDC) (claimed), so can **prevent** presentation or deposition of antigens (Ag), or eliminate Ag already present. Most particularly they are used **treat** or **prevent** HIV infection, or to clear HIV from the body (claimed). (I) also alter the structural organisation of secondary lymphoid tissue that is associated with autoimmune disease such as systemic lupus erythematosus or idiopathic thrombocytopaenia purpura, also autoimmune responses that follow infection, e.g. in cases of Chagas' or Lyme disease. A dose of 1 mg/kg is a typical starting point for optimising **treatment**. (I) is administered orally, by injection, topically, rectally, or from implants.

ADVANTAGE - (I) bind **LT beta R** without interfering with signalling through the tumour necrosis factor receptor (TNF-R), so act selectively on **antibody** responses. They should thus lack the side effects associated with non-specific

immunosuppressants.
Dwg.0/7

L31 ANSWER 33 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 14
ACCESSION NUMBER: 1998406875 EMBASE
TITLE: Both the lymphotoxin and tumor necrosis factor pathways are involved in experimental murine models of colitis.
AUTHOR: Mackay F.; Browning J.L.; Lawton P.; Shah S.A.; Comiskey M.; Bhan A.K.; Mizoguchi E.; Terhorst C.; Simpson S.J.
CORPORATE SOURCE: Dr. F. Mackay, 12 Cambridge Center, Cambridge, MA 02142, United States
SOURCE: Gastroenterology, (1998) Vol. 115, No. 6, pp. 1464-1475.
Refs: 67
ISSN: 0016-5085 CODEN: GASTAB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
AB Background and Aims: Membrane lymphotoxin (LT) α/β, a member of the tumor necrosis factor (TNF) family of immune regulatory molecules, is involved both in the development of secondary lymphoid tissues and the maintenance of organized lymphoid tissues in the adult. Defects observed in the mucosal immune system in animals with a genetically disrupted LTα/β pathway coupled with the expression of LTα/β in activated T cells motivated an examination of the importance of this pathway in experimental colitis. Methods: Soluble **LTβ receptor** (**LT.beta.R**) immunoglobulin fusion protein was used to inhibit the LTα/β/light axis in two independent rodent models of colitis: CD45RB(hi) CD4+-reconstituted SCID mice and bone marrow- transplanted tgε26 mice (BM → tgε26). Results: **Treatment** with **LT. beta.R** immunoglobulin attenuated the development of both the clinical and histological manifestations of the disease in these two murine models of colitis. Given the success of TNF inhibitors in the **treatment** of human Crohn's disease, the effects of **LT.beta.R** immunoglobulin have been compared with **antibody** to TNF in the BM → tgε26 model, and both **treatments** were equally efficacious. Conclusions: The LT pathway plays a role in the development of colitis as important as that of the TNF system and, therefore, represents a potential novel intervention point for the **treatment** of inflammatory bowel disease.

L31 ANSWER 34 OF 44 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 15
ACCESSION NUMBER: 1998262227 EMBASE
TITLE: Lymph node genesis is induced by signaling through the lymphotoxin β receptor.
AUTHOR: Rennert P.D.; James D.; Mackay F.; Browning J.L.; Hochman P.S.
CORPORATE SOURCE: P.D. Rennert, Department of Immunology, Inflammation

Biogen Incorporated, Cambridge, MA 02142, United States
SOURCE: Immunity, (1998) Vol. 9, No. 1, pp. 71-79.
Refs: 47
ISSN: 1074-7613 CODEN: IUNIEH
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19980827
Last Updated on STN: 19980827

AB We investigated lymphotoxin (LT) and TNF function in lymph node genesis and cellular organization by manipulating **LT.beta.-R** and TNF-R signaling. Lymph nodes developed in LTα(-/-) mice **treated** in utero with agonist anti-**LTβ -R** monoclonal **antibody.** Thus, **LTβ -R** signaling mediates lymph node genesis. Surprisingly, mucosal lymph nodes that can develop independently of LTα/ **LTβ -R** interaction were generated. Normal mice **treated** in utero with **LTβ -R**-Ig and TNF-R55-Ig or anti-TNF lacked all lymph nodes, indicating that TNF signaling contributes to lymph node genesis. Lymph nodes generated in LTα(-/-) mice had disrupted cellular organization. Therefore, **LTβ -R** signaling during gestation is not sufficient to establish normal cellular microarchitecture. We conclude that LT and TNF play critical roles in the genesis and cellular organization of lymph nodes.

L31 ANSWER 35 OF 44 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
DUPLICATE 16

ACCESSION NUMBER: 1997-435162 [40] WPIDS
DOC. NO. CPI: C1997-139663
TITLE: Tumour necrosis factor receptor associated factor family protein, TRAF5 - useful to study signal transduction in tumour necrosis factor receptor family.
DERWENT CLASS: B04 D16
INVENTOR(S): NAKANO, H; NAKATA, M; OKUMURA, K; YAGITA, H
PATENT ASSIGNEE(S): (SUME) SUMITOMO ELECTRIC IND CO; (OKUM-I) OKUMURA K
COUNTRY COUNT: 20
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9731110	A1	19970828	(199740)*	JA	69
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: JP US					
EP 882790	A1	19981209	(199902)	EN	
R: CH DE FR GB LI					
JP 09529995	X	19990427	(199927)		
US 6426403	B1	20020730	(200254)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9731110	A1	WO 1997-JP512	19970224
EP 882790	A1	EP 1997-903599	19970224

		WO 1997-JP512	19970224
JP 09529995	X	JP 1997-529995	19970224
		WO 1997-JP512	19970224
US 6426403	B1 CIP of	WO 1997-JP512	19970224
		US 1998-138277	19980818

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 882790	A1 Based on	WO 9731110
JP 09529995	X Based on	WO 9731110

PRIORITY APPLN. INFO: JP 1996-34674 19960222
AN 1997-435162 [40] WPIDS
AB WO 9731110 A UPAB: 19971006
TRAF5, a member of the tumour necrosis factor (TNF) receptor associated factor family, is new, where TRAF5: (i) has a coiled-coil domain and a leucine zipper motif; and (ii) binds to **lymphotoxin beta receptor** and to CD30, but not to CD40 or TNF receptor 2. Also claimed are: (1) mouse and human DNA sequences encoding TRAF5; (2) polynucleotides containing at least twelve consecutive bases from the DNA; (3) **antibodies** against TRAF5; (4) vectors containing all or part of the DNA encoding TRAF5; (5) host organisms containing these vectors; and (6) antisense polynucleotides corresponding to all or part of the DNA encoding TRAF5.

USE - TRAF5 and its corresponding DNA are useful for the investigation of the signal transducer system of the TNF receptor family and the functions of TRAF proteins. They can also be used as probes for research and diagnostic purposes, and investigation of the specific applications of potential **therapeutic** agents.

Dwg.0/11

L31 ANSWER 36 OF 44 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 1997-132373 [12] WPIDS
DOC. NO. NON-CPI: N1997-109308
DOC. NO. CPI: C1997-042711
TITLE: Compositions comprising lymphotoxin-beta receptor blocking agent - used to treat auto immune diseases, e.g. sclerosis, insulin-dependent diabetes, etc..
DERWENT CLASS: B04 D16 S03
INVENTOR(S): BENJAMIN, C D; BROWNING, J L; HOCHMAN, P S
PATENT ASSIGNEE(S): (BIOJ) BIOGEN INC; (BIOJ) BIOGEN IDEC MA INC; (BENJ-I) BENJAMIN C D; (BROW-I) BROWNING J L; (HOCH-I) HOCHMAN P S
COUNTRY COUNT: 73
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9703687	A1	19970206	(199712)*	EN	76
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG					
W: AL AM AT AU AZ BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN					
AU 9665912	A	19970218	(199723)		
NO 9800172	A	19980323	(199822)		

EP 840616	A1	19980513	(199823)	EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT SE SI				
FI 9800122	A	19980319	(199826)	
CN 1195294	A	19981007	(199908)	
HU 9802483	A2	19990301	(199916)	
CZ 9800172	A3	19990512	(199925)	
US 5925351	A	19990720	(199935)	
BR 9609716	A	19990706	(199938)	
JP 11510488	W	19990914	(199948)	69
MX 9800624	A1	19980401	(200004)	
AU 715407	B	20000203	(200016)	
KR 99035805	A	19990525	(200032)	
AU 2000027793	A	20000622	(200036)#	
NZ 313441	A	20000728	(200043)	
SK 9800068	A3	20001009	(200056)	
NZ 503818	A	20010831	(200157)	
US 6403087	B1	20020611	(200244)	
AU 748656	B	20020606	(200249)#	
US 6669941	B1	20031230	(200402)	
EP 840616	B1	20041013	(200467)	EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT SE SI				
MX 216679	B	20031002	(200467)	
DE 69633624	E	20041118	(200476)	
EP 1488799	A2	20041222	(200501)	EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT SE SI				
US 2005037003	A1	20050217	(200514)	
ES 2225889	T3	20050316	(200525)	
KR 2004107513	A	20041220	(200526)	
CN 1607005	A	20050420	(200554)	

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9703687	A1		WO 1996-US12010	19960719
AU 9665912	A		AU 1996-65912	19960719
NO 9800172	A		WO 1996-US12010	19960719
			NO 1998-172	19980114
EP 840616	A1		EP 1996-925393	19960719
			WO 1996-US12010	19960719
FI 9800122	A		WO 1996-US12010	19960719
			FI 1998-122	19980120
CN 1195294	A		CN 1996-196770	19960719
HU 9802483	A2		WO 1996-US12010	19960719
			HU 1998-2483	19960719
CZ 9800172	A3		WO 1996-US12010	19960719
			CZ 1998-172	19960719
US 5925351	A		US 1995-505606	19950721
BR 9609716	A		BR 1996-9716	19960719
			WO 1996-US12010	19960719
JP 11510488	W		WO 1996-US12010	19960719
			JP 1997-506919	19960719
MX 9800624	A1		MX 1998-624	19980121
AU 715407	B		AU 1996-65912	19960719
KR 99035805	A		WO 1996-US12010	19960719
			KR 1998-700464	19980121
AU 2000027793	A	Div ex	AU 1996-65912	19960719
			AU 2000-27793	20000414
NZ 313441	A		NZ 1996-313441	19960719

Searcher : Shears 571-272-2528

			WO 1996-US12010	19960719
SK 9800068	A3		WO 1996-US12010	19960719
			SK 1998-68	19960719
NZ 503818	A	Div ex	NZ 1996-313441	19960719
			NZ 1996-503818	19960719
US 6403087	B1	CIP of	US 1995-505606	19950721
			WO 1996-US12010	19960719
			US 1998-166	19980608
AU 748656	B	Div ex	AU 1996-65912	19960719
			AU 2000-27793	20000414
US 6669941	B1	Cont of	US 1995-505606	19950721
			US 1999-303262	19990430
EP 840616	B1		EP 1996-925393	19960719
			WO 1996-US12010	19960719
		Related to	EP 2004-17208	19960719
MX 216679	B		WO 1996-US12010	19960719
			MX 1998-624	19980121
DE 69633624	E		DE 1996-633624	19960719
			EP 1996-925393	19960719
			WO 1996-US12010	19960719
EP 1488799	A2	Div ex	EP 1996-925393	19960719
			EP 2004-17208	19960719
US 2005037003	A1	CIP of	US 1995-505606	19950721
		Div ex	WO 1996-US12010	19960719
		Div ex	US 1998-166	19980608
			US 2002-77406	20020215
ES 2225889	T3		EP 1996-925393	19960719
KR 2004107513	A		KR 2004-717609	20041102
CN 1607005	A	Div ex	CN 1996-196770	19960719
			CN 2004-7059	19960719

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9665912	A	Based on	WO 9703687
EP 840616	A1	Based on	WO 9703687
HU 9802483	A2	Based on	WO 9703687
CZ 9800172	A3	Based on	WO 9703687
BR 9609716	A	Based on	WO 9703687
JP 11510488	W	Based on	WO 9703687
AU 715407	B	Previous Publ.	AU 9665912
		Based on	WO 9703687
KR 99035805	A	Based on	WO 9703687
AU 2000027793	A	Div ex	AU 715407
NZ 313441	A	Based on	WO 9703687
NZ 503818	A	Div ex	NZ 313441
US 6403087	B1	CIP of	US 5925351
		Based on	WO 9703687
AU 748656	B	Previous Publ.	AU 2000027793
		Div ex	AU 715407
US 6669941	B1	Cont of	US 5925351
EP 840616	B1	Based on	WO 9703687
MX 216679	B	Based on	WO 9703687
DE 69633624	E	Based on	EP 840616
		Based on	WO 9703687
EP 1488799	A2	Div ex	EP 840616
US 2005037003	A1	CIP of	US 5925351
		Div ex	US 6403087

Searcher : Shears 571-272-2528

ES 2225889 T3 Based on EP 840616

PRIORITY APPLN. INFO: US 1995-505606 19950721; AU
2000-27793 20000414; US
1998-166 19980608; US
1999-303262 19990430; US
2002-77406 20020215

AN 1997-132373 [12] WPIDS

AB WO 9703687 A UPAB: 20050915

A pharmaceutical composition which comprises a **therapeutically** effective amount of a **LT- beta -R** blocking agent and a pharmaceutically acceptable carrier is new. Also claimed are: (1) a method for selecting a **LT- beta -R** blocking agent blocking agent, comprising: (a) culturing tumour cells in the presence of an effective amount of at least one **LT- beta -R** activating agent and a putative **LT- beta -R** blocking agent; and (b) determining whether the putative **LT- beta -R** blocking agent decreases the anti-tumour activity of the **LT- beta -R** activating agent; (2) a method for inhibiting **LT- beta -R** signalling without inhibiting TNF signalling comprising administering an effective amount of a **LT- beta -R** blocking agent; and (3) a method of **treating** inflammatory bowel syndrome comprising administering an **LT- beta -R** fusion protein, pref. a fusion of **LT-beta -R** and an **immunoglobulin Fc** domain.

USE - The **LT- beta -R** blocking agents may be used to **treat** a Th1 cell-mediated immune response which contributes to a delayed type hypersensitivity reaction, pref. contact, tuberculin-type or granulomatous hypersensitivity. The **LT- beta -R** blocking agents may be used in the **treatment** of graft-vs-host disease and organ rejection. They are especially used in the **treatment** of an autoimmune disorder selected from multiple sclerosis, insulin-dependent diabetes, sympathetic ophthalmia, uveitis and psoriasis (claimed). The **LT- beta -R** blocking agents will be useful in **treating** conditions that are exacerbated by the activities of Th-1 type cytokines. The ability to selectively or partially block the **LT- beta -R** pathway may be useful in **treatment** of abnormal lymphoid organ development associated with mis- or over-expression of signalling by the **LT- beta -R** pathway. The **LT- beta -R** blocking agents may be used in the **treatment** of infection by Listeria, Toxoplasma and Mycobacterium tuberculosis.

ADVANTAGE - The **LT- beta -R** blocking agents are capable of selectively inhibiting Th1 and not Th2 cell-dependent immune effector mechanisms. As Th1 cytokines can inhibit Th2 cell-dependent responses, **LT- beta -R** blocking agents may also indirectly stimulate certain Th2 cell-dependent responses which are normally inhibited by Th1-induced cytokines.

Dwg.10/10

L31 ANSWER 37 OF 44 TOXCENTER COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:138412 TOXCENTER
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DOCUMENT NUMBER: CA12615198559A
TITLE: Soluble **lymphotoxin-β receptors** and anti-lymphotoxin receptor and ligand **antibodies**, as **therapeutic** agents for the **treatment** of immunological disease
AUTHOR(S): Browning, Jeffrey L.; Benjamin, Christopher D.; Hochman, Paula S.
CORPORATE SOURCE: ASSIGNEE: Hochman, Paula S.
PATENT INFORMATION: WO 973687 A1 6 Feb 1997
SOURCE: (1997) PCT Int. Appl., 75 pp.
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AB This invention relates to compns. and methods comprising "**lymphotoxin-β receptor** blocking agents", which block **lymphotoxin-β receptor** signalling. **Lymphotoxin-β receptor** blocking agents are useful for **treating** lymphocyte-mediated immunol. diseases, and more particularly, for inhibiting Th1 cell-mediated immune responses, e.g. delayed type hypersensitivity, contact hypersensitivity, tuberculin-type hypersensitivity, granulomatous, organ transplant rejection, and others. This invention also relates to the use of **antibodies** directed against either the **lymphotoxin-β receptor** or its ligand, surface lymphotoxin, that act as **lymphotoxin-β receptor** blocking agents. A novel screening method for selecting soluble receptors, **antibodies** and other agents that block **LT-beta. receptor** signalling is provided.

L31 ANSWER 38 OF 44 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 17
ACCESSION NUMBER: 1997:177352 BIOSIS
DOCUMENT NUMBER: PREV199799469065
TITLE: Lymphotoxin-beta receptor signaling complex: Role of tumor necrosis factor receptor-associated factor 3 recruitment in cell death and activation of nuclear factor kappa-B.
AUTHOR(S): Van Arsdale, Todd L.; Vanarsdale, Sammee L.; Force, Walker R.; Walter, Barbara N.; Mosialos, George; Kieff, Elliott; Reed, John C.; Ware, Carl F. [Reprint author]
CORPORATE SOURCE: Division Molecular Immunol., La Jolla Inst. Allergy Immunol., 10355 Science Center Drive, San Diego, CA 92121, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1997) Vol. 94, No. 6, pp. 2460-2465.
CODEN: PNASA6. ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Apr 1997
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AB The binding of heterotrimeric lymphotoxin, LT-alpha-1-beta-2, to the

LT-beta receptor (**LT-beta-R**), a member of the tumor necrosis factor receptor (TNFR) superfamily, induces nuclear factor kappa-B (NF-kappa-B) activation and cell death in HT29 adenocarcinoma cells. We now show that **treatment** with LT-alpha-1-beta-2 or agonistic **LT-beta-R antibodies** causes rapid recruitment of TNFR-associated factor 3 (TRAF3) to the **LT-beta-R** cytoplasmic domain. Further, stable overexpression of a TRAF3 mutant that lacks the RING and zinc finger domains inhibits **LT-beta-R**-mediated cell death. The inhibition is specific for **LT-beta-R** cell death signaling, since NF-kappa-B activation by LT-alpha-1-beta-2 and Fas-mediated apoptosis are not inhibited in the same cells. The mutant and endogenous TRAF3s are both recruited at equimolar amounts to the **LT-beta-R**, suggesting that the mutant disrupts the function of the signaling complex. These results implicate TRAF3 as a critical component of the **LT-beta-R** death signaling complex and indicate that at least two independent signaling pathways are initiated by **LT-beta-R** ligation.

L31 ANSWER 39 OF 44 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 18

ACCESSION NUMBER: 1997:439588 BIOSIS
DOCUMENT NUMBER: PREV199799738791
TITLE: Lymphotoxin but not tumor necrosis factor functions to maintain splenic architecture and humoral responsiveness in adult mice.
AUTHOR(S): Mackay, Fabienne [Reprint author]; Majeau, Gerard R.; Lawton, Pornsri; Hochman, Paula S.; Browning, Jeffrey L.
CORPORATE SOURCE: Biogen, 12 Cambridge Center, Cambridge, MA 02142, USA
SOURCE: European Journal of Immunology, (1997) Vol. 27, No. 8, pp. 2033-2042.
CODEN: EJIMAF. ISSN: 0014-2980.
DOCUMENT TYPE: Article
LANGUAGE: English
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AB To compare the function of the tumor necrosis factor (TNF) and lymphotoxin (LT)alpha/beta systems in the mature immune system, these two pathways were blocked with soluble receptor-immunoglobulin (R-Ig) fusion proteins in normal adult mice. Inhibition of LT-alpha/beta signaling using **LT-beta-R**-Ig or a blocking monoclonal **antibody** against murine LT-beta had profound effects. The spleen lacked discrete B cell follicles and the marginal zone was altered. Less marked changes were detected in lymph nodes. LT-alpha/beta inhibition also **prevented** germinal center formation in the spleen and impaired Ig production in response to sheep red blood cells (SRBC) immunization. These results show that the LT-alpha/beta system is required for the maintenance of splenic architecture and normal immune responses, and not simply for the development of peripheral immune organs during ontogeny. In contrast, inhibition of the TNF/LT-alpha pathway with TNF-R55Ig did not affect the splenic architecture or the anti-SRBC response. Splenic defects and impaired **antibody** responses are seen in TNF-deficient mice, suggesting that TNF is important during development. Therefore relative to TNF, the LT system has the dominant influence on splenic